ASSESSMENT REPORT ON

ACETONE

FOR DEVELOPING AMBIENT AIR QUALITY OBJECTIVES

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FOREWORD

Alberta Environment maintains Ambient Air Quality Objectives[1] to support air quality management in Alberta. Alberta Environment currently has ambient objectives for more than thirty substances and five related parameters. These objectives are periodically updated and new objectives are developed as required.

With the assistance of the Clean Air Strategic Alliance, a multi-stakeholder workshop was held in October 2000 to set Alberta's priorities for the next three years. Based on those recommendations and the internally identified priority items by Alberta Environment, a three-year work plan ending March 31, 2004 was developed to review four existing objectives, create three new objectives for three families of substances, and adopt six new objectives from other jurisdictions.

In order to develop a new three-year work plan, a multi-stakeholder workshop was held in October 2004. This study was commissioned in preparation for the workshop to provide background information on alternative, science based, and cost effective methods for setting priorities.

This document is one of a series of documents that presents the scientific assessment for these adopted substances.

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[1] **NOTE**: The *Environmental Protection and Enhancement Act*, Part 1, Section 14(1) refers to "ambient environmental quality objectives" and uses the term "guidelines" in Section 14(4) to refer to "procedures, practices and methods for monitoring, analysis and predictive assessment." For consistency with the *Act*, the historical term "ambient air quality guidelines" is being replaced by the term "ambient air quality objectives." This document was prepared as the change in usage was taking place. Consequently any occurrences of "air quality guideline" in an Alberta context should be read as "air quality objective."

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ACRONYMS AND ABBREVIATIONS

AAQC	Ambient Air Quality Criterion
ACGIH	American Conference of Governmental Industrial Hygienists
AENV	Alberta Environment
ATSDR	Agency for Toxic Substances and Disease Registry
CNS	Central Nervous System
DNPH	Dinitrophenylhydrazine
DNSH	Dansylhydrazine
EC	Environment Canada
FTIR	Fourier Transform Infrared Spectrometry
GC/FID/MS	Gas Chromatography/Flame Ionization or Mass Spectrometry Detection
HSDB	Hazardous Substances Database
HPLC	High Performance Liquid Chromatography
HSGCB	High-Surface-Area Graphitized Carbon Black
ICPS	International Programme on Chemical Safety
IRIS	Integrated Risk Information System
LOAEL	Lowest Observable Adverse Effect Level
MRL	Minimum Risk Level
MOE	Ontario Ministry of the Environment
MW	Molecular Weight
NIST	National Institute of Standards and Technology
NIOSH	National Institute for Occupational Safety and Health
NOAEL	No Observable Adverse Effect Level
NPRI	National Pollutant Release Inventory
NTP	National Toxicology Program
OECD	Organization for Economic Cooperation and Development
OEL	Occupational Exposure Limit
OP-FTIR	Open Path Fourier Transform Infrared
OSHA	Occupational Safety and Health Administration
POHC	Principle Organic Hazardous Constituents
POI	Point of Impingement
PPTFE	Porous Polytetrafluoroethylene
STEL	Short-Term Exposure Limit
TLV	Threshold Limit Value
TWA	Time Weighted Average
US EPA	United States Environmental Protection Agency
VOC	Volatile Organic Compound
VOST	Volatile Organic Sampling Train
WHO	World Health Organization

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SUMMARY

Acetone is a clear, colourless liquid, which readily evaporates at ambient temperatures. The majority of worldwide production of acetone is for the synthesis of chemical feedstock methyl methacrylate and Bisphenol A. The low viscosity, high evaporation rate, and miscibility of acetone make it a useful solvent. Acetone is used as a formulating solvent, an intermediate, an extraction solvent, and a precipitation agent.

Upon release to the environment acetone will primarily disperse into air (71% by mass) and water (28.58% by mass). Acetone undergoes atmospheric degradation via photolysis and reaction with hydroxyl radicals; however, cloud cover and air pollution can affect the atmospheric half-life of acetone.

Acetone is present in nearly all organs and tissues within the human body. It is produced as an energy source following the metabolic breakdown and utilization of stored fats. Acetone is excreted in exhaled breath. Other natural sources of acetone air emissions include vegetation (mainly evergreens), volcanic eruptions, forest fires, and oceans.

Anthropogenic emission sources of acetone include chemical and manufacturing industries, vehicle exhaust, biomass and plastics burning, pulping, refuse combustion, tobacco smoke, petroleum production, and landfills. It is also released following the use of certain products including nail polish removers, particle board, carpet backing, paint removers, waxes and polishes, adhesives, detergents and cleaners.

Acetone is produced in the atmosphere by photooxidation of compounds such as propane, propylene oxide, epichlorohydrin, mycene, and other C_4 to C_6 alkenes. In 1999, ambient air concentrations of acetone were well below acceptable levels within cities and near primary emission sources. This resulted in the removal of acetone as a reportable substance for Environment Canada's National Pollutant Release Inventory.

In humans and animals, toxicity endpoints associated with acetone inhalation include acute irritation of the respiratory tract and eye and minor neurological disturbances. Very little chronic inhalation data for humans and animals were identified, likely due to the low chronic toxicity and endogenous nature of acetone. A study was conducted on the effects of a mixture of six volatile organic compounds, including acetone (200 $\mu g/m^3$), on herbaceous plants exposed in open-top chambers for seven weeks. Significant effects on seed production, leaf water content and photosynthetic efficiency were reported in some plant species; however, these effects could not be attributed specifically to acetone.

Standard air monitoring methods for acetone are based on liquid impinger, coated-solid cartridge, sorbent tube, or direct-reading instrument sampling approaches. Widely employed and accepted reference air monitoring methods for acetone have been developed, tested and reported by the US EPA, NIOSH, and OSHA. Emerging monitoring technologies for acetone include passive and automated continuous sampling methods, involving alternative types of sorbents, reagents and sampling and analytical techniques used in conjunction with accepted approaches.

With the exception of Ontario and the ATSDR, all of the agencies identified (*i.e.*, Arizona DEQ, Massachusetts DEP, Michigan DEQ, New Hampshire DES, Texas CEQ, Vermont ANR, and Washington DOE) developed ambient air quality guidelines for acetone based on occupational exposure limits (OELs). These OELs included the ACGIH 15-minute STEL (2,380 mg/m^3), the ACGIH 8-hour TWA OEL (1,780 mg /m3), and the NIOSH 8-hour TWA REL (590 mg/m^3). The OELs were divided by a wide range of safety factors (SF) to develop 1-hour (SF = 100 and 120), 8-hour (SF = 10 and 100), 24-hour (SF=126, 300 and 420), and annual average (SF = 1000) ambient air quality guidelines. In general, the safety factors were applied to adjust for longer exposure periods and to account for sensitive individuals in the general public.

The use of OELs is cautioned in the development of ambient air quality guidelines or objectives. Occupational limits are established for a population of healthy workers (*e.g.*, 17 to 65 years) and are based on workplace information, including limited exposures (40 hours per week), daily breaks, and extended weekend periods in which the body may recover from exposure. In addition, workers sensitive to chemical exposure often leave their positions and may not be represented in clinical or epidemiological studies of chemical effects from occupational exposure.

OELs are not established for continuous exposure and are not an accurate reflection of the sensitivity of individuals who are not found in the workplace (*e.g.*, elderly and infants). It is for these reasons that agencies using occupational limits have a policy of adjusting them downward with the use of SF to derive ambient guidelines. As evident in the wide range of SF used to develop ambient air quality guidelines for acetone, uncertainty exists in terms of whether too little (or too much) safety is inherent in guidelines developed from occupational limits.

1.0 INTRODUCTION

Ambient air quality objectives are established by Alberta Environment as part of the Alberta air quality management system, Section 14 of the *Environmental Protection and Enhancement Act* (AENV, 2000). The purpose of this assessment report was to provide a review of scientific and technical information to assist in evaluating the basis and background for an ambient air quality objective for acetone. The following aspects were examined as part of the review:

- Physical and chemical properties;
- Existing and potential anthropogenic emissions sources in Alberta;
- Effects on humans, animals, and vegetation;
- Monitoring techniques, and;
- Ambient air guidelines and objectives in other Canadian jurisdictions, United States, World Health Organization and New Zealand, and the basis for development and use.

The physical and chemical properties identified for acetone include chemical structure, molecular weight, melting and boiling points, water solubility, density, vapor density, organic carbon partition coefficient, octanol water partition coefficient, vapor pressure, Henry's Law constant, bioconcentration factor, and odour threshold. A discussion of the behaviour of acetone in the environment was also presented.

Existing and potential natural and anthropogenic sources of acetone emissions in Alberta were examined. Acetone was removed as a reportable substance from Environment Canada's National Pollutant Release Inventory in 1999, based on Canadian data indicating that ambient air levels were not of concern to human health and the environment.

Scientific information about the effects of acetone on humans, animals, and vegetation were identified. Toxicity and epidemiology studies were located in peer reviewed evaluations by the U.S. Environmental Protection Agency, the Agency for Toxic Substances and Disease Registry and the World Health Organization. Limited data on the effects of acetone on vegetation were identified following a comprehensive search of ecological databases.

Air sampling and analytical methods for acetone used in practice by regulatory agencies were included in this assessment. Standard air monitoring methods for acetone are based on liquid impinger, coated-solid cartridge, sorbent tube, or direct-reading instrument sampling approaches. Widely employed and accepted reference air monitoring methods for acetone have been developed, tested and reported by the United States Environmental Protection Agency, the National Institute of Occupational Safety and Health, and the Occupational Safety and Health Administration.

Ambient air guidelines for acetone are used by a number of jurisdictions in North America for different averaging-time periods. These guidelines can be developed by using an occupational exposure level and dividing it by safety or adjustment factors, using non-cancer risk assessment procedures, or by using cancer risk assessment procedures. The basis for how these approaches are used by different jurisdiction to develop guidelines was investigated in this report.

2.0 GENERAL SUBSTANCE INFORMATION

Acetone is a clear colourless liquid with an odour described as sweet, fruity (Verschueren, 2001; Genium, 1999) and mint like (Lewis, 1997). This compound will readily evaporate at ambient temperature and is highly flammable (OECD, 1999; NTP, 2003). The physical characteristics of acetone - low viscosity, high evaporation rate and miscibility in water and organic solvents – make it a useful solvent (ATSDR, 1994). Acetone is a reactive chemical and undergoes addition, oxidation-reduction, and condensation reactions to form alcohols, ketals, acids, and amines; it is commercially important for chemical synthesis (IPCS, 1998).

The chemical formula, structure, registry numbers, synonyms, and trade names for acetone are provided in Table 1 (NIST, 2003).

Table 1 Identification of Acetone

Property	Value
Formula	C_3H_6O
Structure	
CAS Registry number	67-64-1
RTECS number[1]	AL3150000
UN number	UN 1090
Synonyms	2-Propanone; β-Ketopropane; Dimethyl ketone; Dimethylformaldehyde; Methyl ketone; Pyroacetic ether; Ketone propane; Acetone oil; Chevron acetone

[1]IPCS, 1998

Acetone is present in almost all organs and tissues within the human body, it is produced as an energy source following the metabolic breakdown and utilization of stored fats and is continuously excreted in urine and exhaled breath (OECD, 1999). Acetone is emitted from several tree species and occurs naturally in plants, including onions, grapes, cauliflower, tomatoes, morning glories, wild mustard, beans, and peas (IPCS, 1998).

Major commercial uses of acetone include chemical feedstock, formulating solvent for commercial products and industrial process solvent. The majority of worldwide production of acetone is for the synthesis of chemical feedstock methyl methacrylate and Bisphenol A (OECD, 1999). Acetone is also used to prepare methyl isobutyl ketone, methyl isobutyl carbinol, isophorone and diacetone alcohol (IPCS, 1998). Acetone is used as a formulating solvent in paints, inks, resins, varnishes, lacquers, surface coatings, paint removers, and automotive care products. This compound is an intermediate and solvent in the manufacture of pharmaceuticals and cosmetics, an extraction solvent for fats and oils and a precipitation agent to purify sugars and starch. Acetone is also used to manufacture cellulose acetate yarn, polyurethane foam, and smokeless gun powder (IPCS, 1998; OECD, 1999).

2.1 Physical, Chemical and Biological Properties

The physical and chemical properties of acetone are summarized in Table 2.

Table 2 Physical and Chemical Properties of Acetone

Property	Value	Reference
Molecular Weight	58.08 g/mole	Verschueren, 2001
Physical State	Liquid	Verschueren, 2001
Melting Point	-94.8°C	HSDB, 2003
Boiling Point	56.2 °C at 1 atm	Verschueren, 2001
Specific gravity (liquid)	0.78996 at 20°C	HSDB, 2003
Specific gravity (gas) (air=1)	2	Verschueren, 2001
Vapor Pressure	181.72 mmHg at 20°C 231.06 mmHg at 25°C	IPCS, 1998
Solubility	Soluble in organic solvents	HSDB, 2003
Solubility in water	Completely miscible at 20°C >100mg/ml at 22°C	OECD, 1999 NTP, 2003
Henry's Law Constant at 25°C	1.87×10^{-5} atm-m^3/mol	HSDB, 2003
Octanol water partition coefficient (Log K_{ow})	-0.24	OECD, 1999; HSDB, 2003
Organic carbon partition coefficient (Log K_{oc})	0.73 0.30 (calculated)	IPCS, 1998 OECD, 1999
Flash Point (closed cup)	-17°C (closed cup) -9°C (open cup)	OECD, 1999
Explosive limits at 25°C	2.6% to 12.8% 2.2% to 13.0 %	IPCS, 1998 OECD, 1999
Autoignition temperature	465°C	OECD, 1999
Odour threshold	9.5 mg/m^3 (detection) 30 to 48 mg/m^3 (absolute) 237 to 332 mg/m^3 (100% recognition)	IPCS, 1998
Bioconcentration factor in fish (BCF)	0.65 (Atlantic Cod)	OECD, 1999
Conversion factors for vapour (at 25°C and 101.3 kPa)	1 ppm = 2.411 mg/m^3 1 mg/m^3 = 0.415 ppm	Verschueren, 2001

2.2 Environmental Fate

Upon release to the environment acetone will primarily disperse into air (71% by mass) and water (28.58% by mass) as determined by level I fugacity modeling analysis (OECD, 1999). In the atmosphere, acetone is present in the vapour phase and can undergo degradation via photolysis and reaction with hydroxyl radicals; cloud cover and air pollution will increase the atmospheric half-life of acetone (IPCS, 1998). Very little acetone is expected to remain in soil; volatilization, leaching and biodegradation are primary soil removal processes for acetone (OECD, 1999; IPCS, 1998; ATSDR, 1994). In water, acetone is completely miscible, readily biodegradable, and will volatilize from water surfaces (IPCS, 1998). Acetone will not significantly adsorb to suspended solids or sediments and is unlikely to bioconcentrate or biomagnify in aquatic or terrestrial food chains (ATSDR, 1994).

A summary of the environmental fate and half-lives for acetone is provided in Table 3 (IPCS, 1998; HSDB, 2003).

Table 3 Environmental Fate of Acetone

System	Fate	Half life
Water	Biodegradation and volaltilization from surface.	Estimated half-lives for model river: 38 hours and model lake: 333 hours. Experimental half-life (volatization) in shallow stream: 8-18 hours.
Soil	Biodegradation, volatilization and leaching to groundwater.	Not expected to remain in soil.
Air	Degradation via photolysis and reaction with hydroxyl radicals.	Atmospheric half-life of 71 days due to reaction with hydroxyl radicals. Atmospheric half-life of 80 days due to photodecomposition. Atmospheric half-life of 22 days due to combined photolysis and reaction with hydroxyl radicals.

3.0 EMISSION SOURCES AND INVENTORIES

3.1 Emission Sources and Ambient Levels

Acetone is emitted to the atmosphere via both natural and anthropogenic sources. According to Singh *et al.* (1994), global emissions of acetone are estimated at 40 to 60 Tg (10^{12} g) per year. Of this amount, secondary formation of acetone is estimated to contribute to approximately 50% of these emissions. Biomass burning, direct biogenic emissions and primary anthropogenic emissions contribute to 26%, 21% and 3% of the global acetone emissions, respectively (Singh *et al.*, 1994). These emissions sources are described in more detail in the following sections.

3.1.1 Natural Sources

Natural sources of acetone to the air include emissions from land vegetation (mainly evergreens) (Janson and de Serves, 2001; Singh *et al.*, 1994), volcanic eruptions (Graedel *et al.*, cited in HSDB, 2003 and ATSDR, 1994), forest fires (Graedel *et al.*, cited in HSDB, 2003 and ATSDR, 1994) and human breath (Conkle *et al.*, Krotoszynski, Trotter *et al.*, cited in ATSDR, 1994). Acetone may also be emitted directly from oceans (Zhou and Mopper, cited in IPCS, 1998) and as a metabolic byproduct from plants and animals (Graedel *et al.*, cited in HSDB, 2003; ATSDR, 1994).

3.1.2 Anthropogenic Sources

Anthropogenic sources of acetone to the atmosphere include evaporative emissions during use as a solvent and intermediate in the chemical and manufacturing industries; emissions from vehicles and emissions from biomass burning (Janson and de Serves, 2001; Singh *et al.*, 1994). Of these, biomass burning is believed to be the largest anthropogenic source (Janson and de Serves, 2001). Other sources include wood burning and pulping (Lipari *et al.*, Graedel *et al.*, Kleindienst *et al.*, cited in IPCS, 1998 and ATSDR, 1994), plastics burning (Hodgkin *et al.*, cited in IPCS, 1998 and ATSDR, 1994), refuse combustion (NAS, cited in IPCS, 1998 and ATSDR, 1994), tobacco smoke (Manning *et al.*, cited in IPCS, 1998 and ATSDR, 1994), petroleum production (Graedel, cited in IPCS, 1998) and landfills (LaRegina *et al.*, Militana and Mauch, Hodgson *et al.*, cited in IPCS, 1998).

Acetone is also produced through photooxidation of compounds such as propane (Janson and de Serves, 2001; Singh and Hanst, Arnold *et al.*, cited in IPCS, 1998 and ATSDR, 1994), propylene oxide, epichlorohydrin (Spicer *et al.*, cited in IPCS, 1998 and ATSDR, 1994), mycene (Arnts and Gay, cited in Singh *et al.*, 1994) and other C_4 to C_6 alkenes (NAS, cited in Singh *et al.*, 1994). Oxidation of α-pinene may also be a large secondary source of acetone (Gu *et al.*, cited in Singh *et al.*, 1994), but no independent corroboration of this acetone production pathway has been found in the literature (Singh *et al.*, 1994).

Emissions of acetone may also result from the use of certain products such as nail polish removers, particle board (Tichenor and Mason, cited in ATSDR, 1994), carpet backing (Hodgson *et al.*, cited in ATSDR, 1994), some paint removers (Hahn and Wershulz, cited in ATSDR, 1994), some waxes and polishes, certain detergents and cleansers (Knoeppel and Shauenburg,

Sack *et al.*, cited in ATSDR, 1994), certain adhesives and some carburetor and choke cleaners (US EPA, cited in ATSDR, 1994).

Acetone is currently not a reportable substance for Environment Canada's National Pollutant Release Inventory (NPRI). Acetone was removed as a reportable substance in 1999, after the US EPA also removed it as a reportable substance to the Toxics Release Inventory (TRI) (Minister of Public Works and Government Services, 1999). The justifications for removing acetone from the list of reportable substances was that, based on Canadian exposure and release data, ambient air levels of acetone in Canadian cities and in the vicinity of manufacturing facilities were not of concern with respect to human exposure and the environment (Minister of Public Works and Government Services, 1999). According to studies, ambient air levels of acetone even in the vicinity of large emitters of acetone were well below acceptable levels (EC, 1999). Recently, there has been some discussion about reintroducing acetone as a reportable substance for NPRI due to the possibility that anthropogenic acetone emissions may be a precursor to ground level ozone (EC, 2003). Environment Canada has decided that acetone will not be reintroduced in 2003 and that more work is needed before deciding to reintroduce it as either an individual substance or as a VOC precursor to ground level ozone (EC, 2003).

3.1.3 Ambient Levels

Ambient levels of acetone in air are summarized in HSDB (2003), IPCS (1998), and ATSDR (1994). Concentrations of acetone in the atmosphere range from 0.5 to 125.4 $\mu g/m^3$ (0.2 to 52.9 ppb) (IPCS, 1998). Ambient air levels of acetone were measured at 1.7 ppb in rural Ontario (Shepson *et al.*, cited in ATSDR, 1994) and 0.38 ppb in clean air (Zhou and Mopper, cited in ATSDR, 1994). Air quality monitoring in the town of Banff, Alberta identified one-hour acetone concentrations in air of 5 and 2.35 $\mu g/m^3$ on November 19 and 22, 2002, respectively; the acetone levels in the Town of Banff were attributed to vehicle emissions (AENV, 2003).

4.0 EFFECTS ON HUMANS, ANIMALS AND VEGETATION

Acetone is one of three ketones produced endogenously (in the body) (ATSDR, 1994; IPCS, 1998). When the body is stressed (fasting, exertion, diabetes) blood acetone concentrations increase, under these conditions, when normal glucose stores are depleted, endogenous acetone acts as an intermediate in the metabolic production of energy (US EPA, 2003).

This assessment focused on adverse health effects associated with acetone inhalation, oral and dermal effects were not reviewed in detail. The primary literature sources for this assessment were the U.S. Environmental Protection Agency (US EPA, 2003; IRIS, 2003) and the Agency for Toxic Substances and Disease Registry (ATSDR, 1994), and, to a lesser extent, the World Health Organization (IPCS, 1998) Environmental Health Criteria Document No. 207.

4.1 Overview of Chemical Disposition

4.1.1 Absorption, Distribution, Metabolism and Excretion

The following is a summary of the chemical disposition of acetone in humans and animal systems focusing on the inhalation route of exposure. Specific details of metabolic pathways and metabolic products are not described unless identified as significant in the assessment of health effects (*i.e.* reactive metabolites are produced).

Acetone is *normally* and continuously produced endogenously (inside the body), mainly in the liver but also in the lungs and kidneys (IPCS, 1998). It is rapidly transported via the blood throughout the entire body; blood borne acetone can cross the placental barrier and has been measured in breast milk (US EPA, 2003; ATSDR, 1994; Gavin *et al.*, LeBaron, Pellizzari *et al.*, Vance, cited in ATSDR, 1994). Once circulated to the body tissues, endogenous acetone can be used as a source of energy. The concentrations found in the body can vary significantly depending on age, nutritional status, and degree of physical activity (Jones, Koeslag *et al.*, Kundu *et al.*, Levy *et al.*, Lewis, Neiman, Paterson *et al.*, Peden, Reichard *et al.*, Rooth and Calstrom, Williamson and Whitelaw, cited in ATSDR, 1994). In humans, conditions such as diabetes, trauma, or alcoholism can result in increased blood and urine acetone concentrations (acetonemia and acetonuria) (US EPA, 2003; Kobayashi *et al.*, Levey *et al.*, Phillips *et al.*, Reichard *et al.*, Rooth, Rooth and Ostenson, Smith *et al.*, Tsukamoto *et al.*, cited in ATSDR, 1994). Endogenous acetone is predominantly eliminated by enzymatic metabolism; a small amount is excreted in exhaled breath or in the urine (US EPA, 2003; IPCS, 1998; Charbonneau *et al.*, Haggard *et al.*, Owen *et al.*, Reichard *et al.*, Wigaeus *et al.*, cited in ATSDR, 1994).

After exogenous (outside the body) exposure, acetone is easily and rapidly absorbed; 30% to 80% of inhaled acetone is absorbed in the lungs and 74% to 83% of ingested acetone by the gastrointestinal tract. The skin also easily absorbs acetone after dermal exposure. Absorption appears to be similar in human and animals and appears to be absorbed mainly in the lungs, not in the nasal passages. A large percentage (75%-80%) of the inhaled dose is absorbed into the blood within 15 minutes after exposure and then, as with endogenous sources, it is rapidly distributed to all the body tissues and organs, particularly those with high water content (US EPA, 2003; ATSDR, 1994; IPCS, 1998). Repeated exposure to acetone does result in bioaccumulation in any body tissues (US EPA, 2003).

Metabolism of acetone occurs largely in the liver and is independent of source (exogenous/endogenous) and route of exposure. Three gluconeogenic pathways appear to be responsible for metabolism in humans and a number of experimental animal species (rats, mice and rabbits). Two pathways operate as the primary routes of metabolism at lower exposure doses, the third pathway becoming more active when the first two become saturated (US EPA, 2003; ATSDR, 1994). Formate, an intermediate metabolite of acetone is nephrotoxic and may be responsible for renal effects reported in rats exposed orally (IPCS, 1998; American Biogenics Corp, Hallier *et al.*, NTP, cited in ATSDR, 1994). Other metabolites of acetone do not appear to be responsible for the adverse health effects associated with acetone exposure (ATSDR, 1994).

The major route of excretion after inhalation exposure is in expired air as either acetone, or carbon dioxide. A small amount is excreted in the urine. Excretion after a single exposure occurs within 20 hours of inhalation and after intermittent exposures within 48-72 hours of the last exposure. Rate of excretion is dependant on the exposure dose, level of physical exercise and other specific conditions of the individual (*e.g.*, age, nutritional status, diabetes, trauma, alcoholism) (ATSDR, 1994; IPCS, 1998; IRIS, 2003; US EPA, 2003).

The mechanism of adverse effects after exposure to exogenous acetone (see Sections 4.3 and 4.4) is unknown. Acetone is highly water-soluble and has lipid solvent properties (a defatting agent). The latter may be responsible for acetone's ability to irritate mucous membranes and interfere with membrane composition (OECD, 1999; Adams and Bayliss, cited in ATSDR, 1994).

4.1.2 Effects on Enzyme Systems

Acetone can induce microsomal enzymes, particularly cytochrome P-450IIE1 that can potentiate the toxicity of other chemicals. Exposure to acetone has been demonstrated to increase the hepatotoxicity of carbon tetrachloride and chloroform (chemicals which have reactive metabolites) due to the enhancement of cytochrome P-450IIE1 and related enzymes (Brady *et al.*, Brown and Hewitt, Charbonneau *et al.*, Folland *et al.*, Hewitt *et al.*, Johansson *et al.*, Kobusch *et al.*, Plaa *et al.*, Plaa and Traiger, Sipes *et al.*, Traiger and Plaa, cited in ATSDR, 1994). Enhanced toxicity of other chemicals has also been attributed to acetone's ability to stimulate microsomal enzymes. For example: hepatotoxicity (acetaminophen, N-nitrosodimethylamine, N-nitrosodiethylamine, thiobenzene, oxygen and chromate); nephrotoxicity (N-(3,5-dichlorophenyl) succinimide); genotoxicity (N-nitrosodimethylamine); hematotoxicity (benzene); and, lethality (acetonitrile) (Chieli *et al.*, Freeman and Hayes, Glatt *et al.*, Hong and Yang, Jeffery *et al.*, Johansson *et al.*, Johansson and Ingelman-Sundberg, Mikalsen *et al.*, Moldeus and Gergely, Liu *et al.*, Lo *et al.*, Lor *et al.*, Schnier *et al.*, Sipes *et al.*, Tindberg and Ingelman-Sundberg, Yoo and Yang, Yoo *et al.*, cited in ATSDR, 1994). Acetone also enhances the toxicity of other chemicals possibly through interaction with the mixed function oxidases, inhibition of alcohol dehydrogenase and/or other pathways not yet identified (ATSDR, 1994; Cunningham *et al.*, Ladefoged and Perbellini, Ladefoged *et al.*, Lam *et al.*, Larson *et al.*, Lo *et al.*, cited in ATSDR, 1994). It is important to note, that the induction of microsomal enzymes is a natural response to chemical exposure and not necessarily an adverse effect (ATSDR, 1994).

4.2 Genotoxicity and Carcinogenicity

The US EPA (IRIS, 2003; US EPA, 2003), ATSDR (1994), or WHO (IPCS, 1998) did not identify any inhalation-specific studies of acetone to determine genotoxicity in humans or animals or carcinogenicity in animals following this route of exposure. Also, no studies on the carcinogenicity of acetone following oral exposure in humans or experimental animals were identified. Acetone is commonly used as a solvent or vehicle control in dermal studies (NTP, Ward *et al.*, Zakova *et al.*, cited in IRIS, 2003).

A single long-term study of workers exposed to methylene chloride and acetone (see Table 8) was published in 1983 (Ott *et al.* and Ott *et al.* cited in ATSDR, 1994 and IRIS, 2003). The control group for this study was exposed to acetone only. The focus of this study was the potential effect of methylene chloride on hematological and circulatory systems; some causes of death (including from malignant neoplasm) were also reported. The incidences of malignant neoplasm (cell type or target organ was not reported) and death in the control group were lower than expected (Ott *et al.* and Ott *et al.* cited in IRIS, 2003).

Acetone was non-tumourigenic when tested alone, as a tumour initiator or as a tumour promoter (in skin painting assays). Although acetone *may* be weakly genotoxic, the majority of *in vitro* genotoxicity assays reviewed were negative (ATSDR, 1994; IPCS, 1998; IRIS, 2003; OECD and US EPA, cited in IRIS, 2003). *In vivo* studies of the potential genotoxicity of acetone after intraperitoneal injections were also negative (Basler, Quarles *et al.*, Kawachi *et al.*, cited in ATSDR, 1994). The majority of *in vitro* genotoxicity studies were negative (IRIS, 2003; DeFlora, Deflora *et al.*, De Marini *et al.*, Ishidate *et al.*, Kawachi *et al.*, Kubinski *et al.*, Menck *et al.*, McCann *et al.*, Rahn *et al.*, Rossman *et al.*, Vasavada and Padayatty, Yamaguchi, cited in ATSDR, 1994). However, a few positive results indicate that acetone *may* have weak genotoxic potential (ATSDR, 1994; Albertini *et al.*, Ishidate *et al.*, Kawachi *et al.*, cited in ATSDR, 1994).

4.3 Acute and Sub-Acute Effects

Acute effects usually occur rapidly as a result of short-term exposures that are of short duration – generally for exposures less than 24 hours. Sub-acute effects usually occur as a result of exposures that are of an intermediate duration – generally for exposures lasting a few days to no greater than one month (Eaton and Klaasson, 1996).

4.3.1 Acute and Sub-Acute Human Effects

Table 4 lists some of the lowest and highest NOAELs (No Observable Adverse Effect Level) and LOAELs (Lowest Observable Adverse Effect Level) reported in the literature from acute human exposures. Table 5 lists some of the lowest and highest NOAELs and LOAELs reported in the literature from sub-acute human exposures.

Table 4 NOAELs and LOAELs For Acute Acetone Inhalation (Human)

Effects Reported[a]	Exposure Period	Air Concentration[2] ppm (mg Acetone/m^3)	Reference
Systemic: Irritation of throat and nose. NOAEL.	3-5 min	200 (475)	Nelson *et al.*, cited in ATSDR, 1994.
Irritation of throat and nose. Less serious LOAEL.	3-5 min	500 (1,188)	Nelson *et al.*, cited in ATSDR, 1994.
Irritation of throat and nose. Less serious LOAEL.	6 hr	100 (236)	Matsushita *et al.*, cited in ATSDR, 1994.
Irritation of throat and lungs. Less serious LOAEL.	2 min-4 hr	12,000 (28,506)	Ross, cited in ATSDR, 1994.
Haematological/Immunological Effects (increased white blood cell count; decreased neutrophil phagocytic activity). Less serious LOAEL.	6 hr	250 (594)	Matsushita *et al.*, cited in ATSDR, 1994.
Haematological/Immunological Effects (increased white blood cell count; decreased neutrophil phagocytic activity). Less serious LOAEL.	6 hr	500 (1,188)	Matsushita *et al.*, cited in ATSDR, 1994.
Haematological Effects. NOAEL.	2 hr	500 (1,188)	DiVincenzo *et al.*, cited in ATSDR, 1994.
Hepatic Effects. NOAEL.	2 hr	500 (1,188)	DiVincenzo *et al.*, cited in ATSDR, 1994.
Renal Effects. NOAEL.	2 hr	500 (1,188)	DiVincenzo *et al.*, cited in ATSDR, 1994.
Neurological: Unconsciousness; dizziness; unsteadiness; confusion; headache. Serious LOAEL.	2 min-4 hr	12,000 (28,506)	Raleigh and McGee, cited in ATSDR, 1994.
Signs of narcosis in 3-6 hrs; loss of righting reflex in 8 hr. Serious LOAEL.	1-8 hr	21,049 (50,000)	Haggard *et al.*, 1994, cited in ATSDR, 1994.

Table 4 NOAELs and LOAELs For Acute Acetone Inhalation (Human)

Effects Reported[1]	Exposure Period	Air Concentration [2] ppm (mg Acetone/m^3)	Reference
Increases in response and % false negatives in auditory discrimination; increased anger and hostility. Less serious LOAEL.	4 hr	237 (563)	Dick *et al.*, cited in IRIS, 2003 and ATSDR, 1994.
Subjective symptoms (tension, tiredness, complaints and annoyance). Less serious LOAEL.	4-8 hr	1000 (2,375)	Seber *et al.*, cited in ATSDR, 1994.
Lack of energy; general weakness. Less serious LOAEL.	6 hr	250 (594)	Matsushita *et al.*, cited in ATSDR, 1994.

[1] NOAEL, Less serious LOAEL and Serious LOAEL as identified by ATSDR (1994) where, "serious effect(s) evoke failure of a biological system and can lead to morbidity or mortality [and] less serious effect(s) are not expected to cause significant dysfunction or death…significance to the organism is not entirely clear" (ATSDR, 1994).

[2] When both units of concentration were not provided in the literature, the following conversion factor and assumptions were used: mg/m^3 x 24.45/MW =ppm; MW=58.08, air at 25°C and 101.3 kPa (760mmHg) (Plog *et al.*, 1996).

Table 5 NOAELs and LOAELs For Sub-Acute Acetone Inhalation (Human)

Effects Reported[a]	Exposure Period	Air Concentration [2] ppm (mg Acetone/m^3)	Reference
Systemic:			
Irritation of throat and nose. Less serious LOAEL.	6 hr/d, 6 d	250 (594)	Matsushita *et al.*, cited in ATSDR, 1994.
Irritation of throat and nose. Less serious LOAEL.	8 hr/d, 2-3 d	901 (2,140)	Raleigh and McGee, cited in ATSDR, 1994.
Irritation of throat and nose. Less serious LOAEL.	8 hr/d , 7 d	1,003 (2,382)	Raleigh and McGee, cited in ATSDR, 1994.
Groups of 4 men. Normal clinical chemistry, haematological analyses, urinanalyses, encephalograms, electrocardiograms and cognitive and pulmonary function tests. 1 wk of fluctuating concentrations. NOAEL	3 or 7.5 hr/d, 4 d/wk, 4 wk 750-1250 ppm for 3 d.	1,250 (2,969)	Stewart *et al.*, cited in US EPA, 2003.
Groups of 2 women. Normal clinical chemistry, haematological analyses, urinanalyses, encephalograms, electrocardiograms and cognitive and pulmonary function tests. NOAEL.	3 or 7.5 hr/d, 4 d.	1,000 (2,375)	Stewart *et al.*, cited in US EPA, 2003.
Neurological:			
NOAEL.	8 hr/d, 2-3 d	901 (2,140)	Raleigh and McGee, cited in ATSDR, 1994.
Headache; light-headedness. Less serious LOAEL.	8 hr/d, 7 d	1,006 (2,390)	Raleigh and McGee, cited in ATSDR, 1994.
Delayed visual reaction time; lack of energy; weakness. Less serious LOAEL.	6 hr/d, 6 d	250 (594)	Matsushita *et al.*, cited in ATSDR, 1994.
Increased visual evoked response amplitude in males on individual days (no consistent pattern observed). 1 wk of fluxuating concentrations LOAEL	3 or 7.5 hr/d, 4 d/wk, 4 wk 750-1250 ppm for 3 d.	1,250 (2,969)	Stewart *et al.*, cited in US EPA, 2003.
Reproductive:			
Shortened menstrual cycle. Less serious LOAEL.	7.5 hr/d, 4 d	1,000 (2,375)	Stewart *et al.*, cited in US EPA, 2003.

[1] NOAEL, Less serious LOAEL and Serious LOAEL as identified by ATSDR (1994) where, "serious effect(s) evoke failure of a biological system and can lead to morbidity or mortality…[and] less serious effect(s) are not expected to cause significant dysfunction or death…significance to the organism is not entirely clear" (ATSDR, 1994).

[2] When both units of concentration were not provided in the literature, the following conversion factor and assumptions were used: mg/m^3 x 24.45/MW =ppm; MW=58.08, air at 25°C and 101.3 kPa (760mmHg) (Plog *et al.*, 1996).

Below is a summary of potential effects associated with acute and sub-acute acetone inhalation in humans. Details regarding exposure concentrations and duration of exposure are included in Tables 4 and 5.

4.3.1.1 Respiratory Effects

The only adverse effect reported in association with inhalation of acetone in humans was irritation of the nose, throat, trachea, and lungs. Some exposed persons reported subjective symptoms such as losing the ability to smell the acetone (Matsushita *et al.*, cited in ATSDR, 1994). More serious effects to the respiratory system were not reported (ATSDR, 1994).

4.3.1.2 Cardiovascular Effects

There have been reports of high pulse rate in patients after exposure to a cast setting solution containing acetone. Acetone was detected in the breath, urine, and blood of these subjects after exposure. In these cases, dermal exposure is also likely to have occurred (Chatterton and Elliot, 1946, Hift and Patel, Pomerantz, Renshaw and Mitchell, cited in ATSDR, 1994).

Another controlled inhalation study revealed no changes in electrocardiogram results after exposure (Stewart *et al.*, cited in ATSDR, 1994).

4.3.1.3 Gastrointestinal Effects

Patients exposed to acetone in a cast setting solution experienced severe vomiting. Blood was reported in the vomitus several hours after vomiting began; this gastrointestinal hemorrhage may have been associated with trauma due to repeated vomiting. Acetone was detected in the breath, urine, and blood of these subjects after exposure. In these cases, dermal exposure is also likely to have occurred (Chatterton and Elliot, 1946, Fitzpatrick and Claire, Harris and Jackson, Hift and Patel, Pomerantz, Renshaw and Mitchell, Strong, cited in ATSDR, 1994).

4.3.1.4 Neurological Effects

Comatose and collapse of patients exposed to acetone vapours in a cast setting solution was described in a number of case reports (Chatterton and Elliot, Fitzpatrick and Claire, Harris and Jackson, Renshaw and Mitchell, Strong, cited in ATSDR, 1994). Dermal exposure was also thought to have occurred in these cases (ATSDR, 1994).

Other neurological effects reported after exposure to acetone vapours include headache, dizziness, weakness, difficulty speaking, depression, drowsiness, fretfulness, irritability, restlessness, uncoordinated hand movement, nystagmus (involuntary movement of the eye ball), and, unconsciousness (at very high concentrations; $\geq$12,000 ppm or 28,506 mg/m^3). Neurological parameters not affected include electroencephalography, choice reaction time, visual viligence, duel task, memory scanning, postural sway, Romberg test, or heel-to-toe test (Dick *et al.*, Hift and Patel, Matsushita *et al.*, Matsushita *et al.*, Pomerantz, Raleigh and McGee, Ross, Seeber and Keisswetter, Seeber *et al.*, Stewart *et al.*, cited in ATSDR, 1994).

Ingestion of acetone has also been observed to produce narcosis in humans (US EPA, 2003; ATSDR, 1994).

The ASTDR (1994) has established an acute inhalation minimum risk level (MRL) for acetone. This MRL is an ATSDR estimate of acute (up to 14 days) inhalation exposure to acetone at or below which a measurable risk of adverse, noncancerous effects is unlikely (ATSDR, 1994). An acute MRL of 62 mg/m^3 is recommended for acetone based on the LOAEL of 563 mg/m^3 reported by Dick and colleagues for neurobehavioral disturbances in humans (ATSDR, 1994). This LOAEL was divided by a 9-fold uncertainty factor to derive the MRL (3-fold for use of a minimal LOAEL and 3-fold for human variability).

4.3.1.5 Reproductive Effects

Three of four women volunteers exposed to 1,000 ppm (2,375 mg/m^3) acetone for 7.5 hours were reported to have premature periods (Stewart *et al.*, cited in ATSDR, 1994).

4.3.1.6 Other Effects

Studies of human volunteers reported no hepatic or renal effects associated with short-term acetone inhalation (DiVincenzo *et al.*, Stewart *et al.*, cited in ATSDR, 1994). However, acetone has been reported in animal studies to induce liver enzymes (particularly the microsomal monooxygenases such as cytochrome P450 enzymes) and potential hepatotoxicity of other chemicals (Brondeau *et al.*, Vainio and Zitting, cited in ATSDR, 1994). See Sections 4.1 and 4.3.2.3 for more details of this effect. Induction of hepatic microsomal enzymes is a normal response to xenobiotic exposure (ATSDR, 1994).

Volunteers exposed to acetone were reported to have statistically significant changes in immunological parameters (increased white blood cell and eosinophil counts, and decreased neutrophil phagocytic activity); no changes were reported in the lower dose group (Matsushita *et al.*, cited in ATSDR, 1994). DiVincenzo *et al.*, (ATSDR, 1994) reported no hematological changes in exposed volunteers.

Irritation of the eye, with no permanent damage, has been reported by persons exposed occupationally to acetone and by volunteers in controlled exposure studies (Raleigh and McGee, Matsushita *et al.*, Nelson *et al.*, Ross, Sallee and Sappington, cited in ATSDR, 1994). Ocular irritation is considered to be due to direct exposure of the eye to acetone vapour, not due to inhalation (ATSDR, 1994).

4.3.2 Acute and Sub-Acute Animal Effects

Table 6 lists some of the lowest and highest NOAELs and LOAELs reported in the literature from acute animal exposures. Table 7 lists some of the lowest and highest NOAELs and LOAELs reported in the literature from sub-acute animal exposures.

Table 6 NOAELs and LOAELs For Acute Acetone Inhalation (Experimental Animals)

Effects Reported[a]	Exposure Period	Air Concentration[2] ppm (mg Acetone/m^3)	Species	Reference
Death:				
1 of 6 animals died. Serious LOAEL.	4 hr	16,000 (38,007)	Rats	Smyth *et al.*, cited in ATSDR, 1994.
50% animals died. Serious LOAEL.	4 hr	31,994 (76,001)	Rats	Pozzani *et al.*, cited in ATSDR, 1994.
50% animals died. Serious LOAEL.	8 hr	21,091 (50,101)	Rats	Pozzani *et al.*, cited in ATSDR, 1994.
5 of 5 animals died. Serious LOAEL.	3 hr	50,600 (120,198)	Rats	Bruckner and Peterson, cited in ATSDR, 1994.
8 of 8 animals died. Serious LOAEL.	3-4 hr	50,000 (118,773)	Guinea Pigs	Specht *et al.*, cited in ATSDR, 1994.
8 of 9 animals died. Serious LOAEL.	22-26 hr	20,000 (47,509)	Guinea Pigs	Specht *et al.*, cited in ATSDR, 1994.
5 of 5 animals died. Serious LOAEL.	48 hr	10,000 (23,755)	Guinea Pigs	Specht *et al.*, cited in ATSDR, 1994.
Systemic:				
Respiratory. NOAEL.	30 min	6,000 (14,253)	Mice	Schaper and Brost, cited in ATSDR, 1994.
Respiratory (pulmonary congestion and haemorrhage). Renal (congestion and distension of glomeruli). Other (congestion and distension of spleen). All serious LOAELs.	3-8.75 hr	50,000 (118,773)	Guinea Pigs	Specht *et al.*, cited in ATSDR, 1994.
Respiratory (marked pulmonary congestion and haemorrhage). Hepatic (fatty liver in animals that died). Renal (distension of glomeruli). Other (marked congestion and haemorrhage of spleen). All serious LOAELs.	22-26 hr	20,000 (47,509)	Guinea Pigs	Specht *et al.*, cited in ATSDR, 1994.
Respiratory (lung congestion in animals that died). Hepatic (fatty liver in animals that died). Renal (tubular distension). Other (congestion of spleen). All serious LOAELs.	48 hr	10,000 (23,755)	Guinea Pigs	Specht *et al.*, cited in ATSDR, 1994.
Respiratory irritation. Less serious LOAEL.	10 min	77,516 (184,137)	Mice	Kane *et al.*, cited in ATSDR, 1994.
Hepatic (mild fatty deposition). Less serious LOAEL.	3-8.75 hr	50,000 (118,773)	Guinea Pigs	Specht *et al.*, cited in ATSDR, 1994.

Table 6 NOAELs and LOAELs For Acute Acetone Inhalation (Experimental Animals)

Effects Reported[a]	Exposure Period	Air Concentration[2] ppm (mg Acetone/m^3)	Species	Reference
Neurological: NOAEL	5 min-8 hr	4,210 (10,001)	Rat	Haggard *et al*., cited in ATSDR, 1994.
CNS depression (unconditioned performance and reflex tests). Serious LOAEL.	3 hr	12,600 (29,931)	Rat	Bruckner and Peterson, cited in ATSDR, 1994.
Concentration dependant CNS depression (recovery apparent 9 hours after exposure). LOAEL.	3 hr	19,000 (45,134)	Rat	Bruckner and Peterson, cited in US EPA, 2003.
Concentration dependant CNS depression (recovery apparent 21 hours after exposure). LOAEL.	3 hr	25,300 (60,100)	Rat	Bruckner and Peterson, cited in US EPA, 2003.
Signs of narcosis, loss of coordination in 100-250 min. Serious LOAEL.	5 min-8 hr	10,524 (25,000)	Rat	Haggard *et al*., cited in ATSDR, 1994.
Narcosis; coma; paralysis. Serious LOAEL.	25 min-23.4 hr	21,800 (51,785)	Guinea Pig	Specht *et al*., cited in ATSDR, 1994.
NOAEL	4 hr	2,032 (4827)	Mice	DeCeaurriz *et al*., cited in ATSDR, 1994.
NOAEL	24 hr	1,000 (2375)	Mice	Glowa and Dews, cited in ATSDR, 1994.
39% decrease in duration of immobility in behavioural despair swimming test. Serious LOAEL.	4 hr	2,580 (6129)	Mice	DeCeaurriz *et al*., cited in ATSDR, 1994.
Drowsiness; staggering; prostration; clonic movements of hind legs; deep narcosis. Serious LOAEL.	4 hr	16,839 (40,000)	Mice	Mashbitz *et al*., cited in ATSDR, 1994.
Severe Narcosis. Serious LOAEL.	6 hr	11,000 (26,130)	Mice	NTP, cited in ATSDR, 1994.
10% decreased response to food presentation n a fixed interval operant behavioural test. Serious LOAEL.	24 hr	3,000 (7126)	Mice	Glowa and Dews, cited in ATSDR, 1994.

[1]NOAEL, Less serious LOAEL and Serious LOAEL as identified by ATSDR (1994) where, "serious effect(s) evoke failure of a biological system and can lead to morbidity or mortality …[and] less serious effect(s) are not expected to cause significant dysfunction or death…significance to the organism is not entirely clear" (ATSDR, 1994).

[2] When both units of concentration were not provided in the literature, the following conversion factor and assumptions were used: mg/m^3 x 24.45/MW =ppm; MW=58.08, air at 25°C and 101.3 kPa (760mmHg) (Plog *et al*., 1996).

Table 7 NOAELs and LOAELs For Sub-Acute Acetone Inhalation (Experimental Animals)

Effects Reported[a]	Exposure Period	Air Concentration [2] ppm (mg Acetone/m^3)	Species	Reference
Systemic:				
Significantly reduced body weight, uterine weight and extragestational weight gain. NOAEL.	6 hr/d, 14 d Gestational day 6-19	2,200 (5,226)	Rat	NTP (or Mast *et al.*) cited in IRIS, 2003 and ATSDR, 1994.
Body weight gain. NOAEL.	4 hr/d, 5 d/wk 2 wk,	16,000 (38,007)	Rat	Goldberg *et al.*, cited in US EPA, 2003 and ATSDR, 1994.
Significantly reduced body weight, uterine weight and extra-gestational weight gain. Less serious LOAEL.	6 hr/d, 14d Gestational day 6-19	11,000 (26,130)	Rat	NTP (or Mast *et al.*) cited in IRIS, 2003 and ATSDR, 1994.
Serum SGOT activity, LDH activity, BUN and liver triglyceride levels. Microscopic assessment of liver, brain, heart and kidney cells. NOAEL.	3 h/d, 5 d/wk, 8 wk,	19,000 (45,106)	Rat	Bruckner and Peterson, cited in US EPA, 2003.
Respiratory. NOAEL.	5 d, 30 min/d	6,000 (14,253)	Mice	Schaper and Brost, cited in. ATSDR, 1994.
Clinical signs of toxicity, maternal deaths, maternal body weight gain. NOAEL	6 hr/d, 12 d Gestational day 6-17	6,600 (15,678)	Mice	NTP (or Mast *et al.*) cited in IRIS, 2003 and ATSDR, 1994.
Hepatic (significantly increased absolute and relative liver weights of dams). NOAEL.	6 hr/d, 12 d Gestational day 6-17	2,200 (5,226)	Mice	NTP (or Mast *et al.*) cited in IRIS, 2003 and ATSDR, 1994.
Hepatic (significantly increased absolute and relative liver weights of dams). Less serious LOAEL.	6 hr/d, 12 d Gestational day 6-17	6,600 (15,678)	Mice	NTP (or Mast *et al.*) cited in IRIS, 2003 and ATSDR, 1994.
Neurological: NOAEL	4 hr/d, 5 d/wk, 2 wk	3,000 (7,126)	Rat	Goldberg *et al.*, cited in ATSDR, 1994.

Table 7 NOAELs and LOAELs For Sub-Acute Acetone Inhalation (Experimental Animals)

Effects Reported[a]	Exposure Period	Air Concentration [2] ppm (mg Acetone/m^3)	Species	Reference
Ataxia observed in several animals after first exposure, not observed in subsequent exposures.	4 hr/d, 5 d/wk, 2 wk	12,000 (28,506) 16,000 (38,007)	Rat	Goldberg *et al.*, cited in US EPA, 2003.
Inhibition of avoidance behaviour. Serious LOAEL.	4 hr/d, 5 d/wk, 2 wk	6,600 (15,678)	Rat	Goldberg *et al.*, cited in US EPA, 2003 and ATSDR, 1994.
Developmental Effects:				
NOAEL.	6 hr/d, 14 d Gestational days 6-19	2,200 (5,226)	Rat	NTP, cited in ATSDR, 1994.
Decreased fetal weight. Less Serious LOAEL.	6 hr/d, 14 d Gestational days 6-19	11,000 (26,130)	Rat	NTP, cited in ATSDR, 1994.
NOAEL.	6 hr/d, 14 d Gestational days 6-19	2,200 (5,226)	Mice	NTP, cited in ATSDR, 1994.
Accuracy in delayed match-to-sample task. NOAEL.	24 h/d, 7 d	500 (1188)	Baboon	Geller *et al.*, cited in US EPA, 2003.
Changes in number of extra responses compared to animals baseline in a delayed match-to-sample task. LOAEL.	24 h/d, 7 d	500 (1,188)	Baboon	Geller *et al.*, cited in US EPA, 2003.
Significantly increased incidence of late resorption, decreased fetal weight; reduced sternebral ossification. Serious LOAEL.	6 hr/d, 14 d Gestational days 6-19	6000 (14,253)	Mice	NTP, cited in ATSDR, 1994.
Reproductive Effects:				
NOAEL.	6 hr/d, 14 d Gestational days 6-19	11,000 (26,130)	Rat	NTP, cited in ATSDR, 1994.
NOAEL.	6 hr/d, 14 d Gestational days 6-19	6600 (15,678)	Mice	NTP, cited in ATSDR, 1994.

[1] NOAEL, Less serious LOAEL and Serious LOAEL as identified by ATSDR (1994) where, "serious effect(s) evoke failure of a biological system and can lead to morbidity or mortality [and] less serious effect(s) are not expected to cause significant dysfunction or death…significance to the organism is not entirely clear" (ATSDR, 1994).

[2] When both units of concentration were not provided in the literature, the following conversion factor and assumptions were used: mg/m^3 x 24.45/MW =ppm; MW=58.08, air at 25°C and 101.3 kPa (760mmHg) (Plog *et al.*, 1996).

Below is a summary of potential effects associated with acute and sub-acute acetone inhalation in animals. Details regarding exposure concentrations, duration of exposure and animal species studied are included in Tables 6 and 7.

4.3.2.1 Respiratory Effects

Significant respiratory effects were observed in animals when exposed to acetone at concentrations much greater than reported in human studies (≥10,000 ppm or 23,755 mg/m^3) (ATSDR, 1994). These effects included decreased respiratory rate, pulmonary congestions, edema, and hemorrhage of the lungs, which resulted in the death of some animals (Specht *et al.*, Kane *et al.*, cited in ATSDR, 1994).

Schaper and Brost (cited in ATSDR, 1994) reported no change in pulmonary function (time of inspiration, time of expiration, time between breaths, or tidal volume) or lung pathology (lung weight, lung volume displacement, histology) in mice exposed acutely and sub-acutely to 6,000 ppm (14,253 mg/m^3) acetone. Sub-acute inhalation to high concentrations (19,000 ppm or 45,134 mg/m^3) did not produce any treatment related lesions in rat's lungs (Bruckner and Peterson, cited in ATSDR, 1994).

4.3.2.2 Cardiovascular Effects

Exposure to high concentrations of acetone (≥10,000 ppm or 23,755 mg/m^3) resulted in reduced heart rates in guinea pigs, most likely due to acetone's narcotic effect (Specht *et al.*, cited in ATSDR, 1994).

4.3.2.3 Hepatic Effects

Specht *et al.* (cited in ATSDR, 1994) reported fatty deposits in guinea pig livers after inhalation exposure to lethally high doses (20,000 ppm or 47,509 mg/m^3). Liver toxicity was not observed in rats exposed to 19,000 ppm (45,134 mg/m^3) acetone (Bruckner and Peterson, cited in ATSDR, 1994), or in some animal studies of lower exposure concentrations (ATSDR, 1994). Intermittent exposure during gestation resulted in increased maternal liver weights (a sign of maternal toxicity) possibly due to enzyme induction (see below and Section 4.1.2) (NTP, cited in ATSDR, 1994).

Acetone can potentiate the hepatotoxicity of other chemicals through induction of liver microsomal monooxygenases. Acute inhalation in rats has been reported to result in decreased liver free glutathione content, increased concentrations of cytochrome P450, and increased activity of ethyoxyxoumarin O-deethylylase and glutathione S-transferase (Brondeau *et al.*, Vainio and Zitting, cited in ATSDR, 1994). It is important to note that induction of hepatic microsomal enzymes is a normal response to exposure to a xenobiotic (ATSDR, 1994). See Section 4.1.2 for more details of this effect.

4.3.2.4 Neurological Effects

Acute exposure to acetone vapours has been reported to have a narcotic effect in experimental animal studies (Haggard *et al.*, Mashbitz *et al.*, Spect *et al.*, NTP, cited in ATSDR, 1994). Overt signs of narcosis (drowsiness, uncoordinated, loss of autonomic reflexes, unconsciousness, respiratory failure, and death) were reported at high exposure concentrations (≥8,000 ppm or

19,004 mg/m^3) and with increasing duration of exposure. Other specific neurobehavioral effects (CNS depression) were reported at lower concentrations (ATSDR, 1994; Bruchner and Peterson, Geller *et al.*, Goldberg *et al.*, Glowa and Dews, DeCeaurriz, cited in ATSDR, 1994).

Recovery from these neurobehavioral effects was reported with continued exposure or after cessation of exposure. The neurological effects due to acetone inhalation were reversible; no histological changes in the brains of exposed animals were observed (ATSDR, 1994). Acetone ingestion has also been observed to produce narcosis in experimental animals (ATSDR, 1994).

4.3.2.5 Developmental Effects

Rats exposed to high acetone concentrations (11,000 ppm or 26,130 mg/m^3) during gestation had reduced body weight gain (NTP, cited in IRIS, 2003 and ATSDR, 1994). These changes were not reported at lower exposures, in pregnant mice, or in studies of non-pregnant rats (Goldberg *et al.*, cited in ATSDR, 1994; NTP, cited in IRIS, 2003 and ATSDR, 1994).

A study by the National Toxicity Program (NTP, cited in IRIS, 2003 and ATSDR, 1994) observed no reproductive effects in rats or mice exposed to acetone via inhalation. A slight, but statistically significant developmental effect (decreased mean fetal weight) was reported at high exposure doses (11,000 ppm or 26,130 mg/m^3). Maternal toxicity was also observed. In mice, a slight, but statistically significant effect (increased percent late resorptions, decreased mean fetal body weight, increased incidence of sternebral ossifications) was also observed in the 6,000 ppm (14,253 mg/m^3) dose group (NTP, cited in IRIS, 2003 and ATSDR, 1994).

4.3.2.6 Other Effects

Lacrimation was observed in guinea pigs exposed to acetone vapour (Specht *et al.*, cited in ATSDR, 1994).

4.4 Chronic Effects

4.4.1 Chronic Human Effects

Sub-chronic or intermediate exposures are generally one to three months; chronic effects occur as a result of long-term exposures and are of longer duration – generally as repeated exposures for more than 3 months (Eaton and Klaassen, 1996).

The majority of human inhalation exposure data available has been collected after occupational exposures. There are a number of limitations to be considered when using data from people exposed in the work place: i) the person exposed generally is a healthy, young to middle aged, male adult; ii) concurrent exposures to other chemicals are very likely, and; iii) the exposure concentrations are often difficult to define.

Table 8 lists some of the lowest and highest NOAELs and LOAELs reported in the literature.

Table 8 NOAELs and LOAELs For Sub-Chronic and Chronic Acetone Inhalation (Human)

Effects Reported[1]	Exposure Period	Air Concentration [2] ppm (mg Acetone/m^3)	Reference
Systemic:			
Respiratory; cardiovascular; haematological; hepatic; renal. NOAEL.	1-7.5 hr/d, 2-5 d/wk, 6 wk	1,250 (2,969)	Stewart *et al.*, cited in ATSDR, 1994.
Haematological; Hepatic. NOAEL.	8 hr/d, 5 d/wk, 3 mo –23 yr	1,070 (2,542)	Ott *et al.* a,c, cited in US EPA 2003 and ATSDR, 1994.
Manifest Anxiety and Self-rating Depression scales, electrocardiogram, phagocytic activity, haematology, clinical chemistry (male workers only). NOAEL	14.9 and 37.6 yrs	>500 (1,188)	Satoh *et al.*, cited in US EPA, 2003.
Eye irritation, tearing acetone odour, nausea, weight loss (dose-response relationship in male workers). LOAEL	14.9 and 37.6 yrs	<250 (564), 250-500 (594-1,188), >500 (1,188)	Satoh *et al.*, cited in US EPA, 2003.
Neurological Effects:			
Increased visual evoked response. Less serious LOAEL.	1-7.5 hr/d, 2-5 d/wk, 6 wk,	1,250 (2,969)	Stewart *et al.*, cited in ATSDR, 1994.
Narcosis (dose-response relationship in male workers). LOAEL	14.9 and 37.6 yrs	<250 (564), 250-500 (594-1,188), >500 (1,188)	Satoh *et al.*, cited in US EPA, 2003.
Carcinogenic Effects:			
Death due to malignant neoplasms. NOAEL.	3 mo – 23 yr	1,070 (2,542)	Ott *et al.*, a,b, cited in ATSDR, 1994.
Case Reports:			
Drowsiness, eye and throat irritation, dizziness, inebriation, headache (in six workers).	Up to 3h, 7-15 years	309 - 918 (734 – 2,181)	Parmeggiani and Sassi as reviewed by OECD, cited in US EPA, 2003.
Nausea, abdominal pain, headache, vertigo loss of appetite, vomiting and other debilitating symptoms (in four workers).	Not described.	84 – 147 (200 – 349)	Parmeggiani and Sassi as reviewed by OECD, cited in US EPA, 2003.

[1] NOAEL, Less serious LOAEL and Serious LOAEL as identified by ATSDR (1994), where "serious effect(s) evoke failure of a biological system and can lead to morbidity or mortality [and] less serious effect(s) are not expected to cause significant dysfunction or death…significance to the organism is not entirely clear" (ATSDR, 1994).

[2] When both units of concentration were not provided in the literature, the following conversion factor and assumptions were used: mg/m^3 x 24.45/MW =ppm; MW=58.08, air at 25°C and 101.3 kPa (760mmHg) (Plog *et al.*, 1996).

Few studies of chronic acetone inhalation in humans were identified (ATSDR, 1994; IPCS, 1998); this may be due to its low toxicity and endogenous availability (IPCS, 1998). Below is a summary of potential effects associated with chronic acetone inhalation. Details regarding exposure concentrations and duration of exposure are included in Table 8.

4.4.1.1 Respiratory Effects

Sporadic throat irritation was the only respiratory effects reported in volunteers exposed sub-chronically to acetone (Stewart *et al.*, cited in ATSDR, 1994).

4.4.1.2 Reproductive and Developmental Effects

A number of reproductive effects (pregnancy complications, miscarriage and toxicosis) and developmental effects (intrauterine fetal asphyxia, decreased neonatal weight and length) were reported in a study of women exposed to acetone in a Russian factory (Nizyaeva, cited in ATSDR, 1994). However, no conclusions could be made from this report due to other uncontrolled factors in the study (number of women, age, smoking history, alcohol use), nor was a description of the statistical analysis was provided (ATSDR, 1994). Another occupational study of women found no change in pregnancy outcome associated with inhalation of acetone (Axelsson *et al.*, cited in ATSDR, 1994).

4.4.1.3 Neurological Effects

Acetone exposure resulted in central and peripheral neurological effects in chronically (14 and 36 years) exposed workers (Mitran *et al.*, cited in IRIS, 2003). Reports of mood disorders, irritability, memory and sleep problems, headache, hand or feet numbness, eye and/or nose irritation, aches and pains, nausea and abdominal pain were marginally more frequent than in control group. Statistically significant changes in motor nerve conduction and nerve velocity were reported in the exposed group. However, IRIS (2003) and US EPA (2003) report that the Mitran *et al.* study does not adequately account for confounding factors and concludes that the data is not useful for determining a chronic exposure limit (Boyes and Herr, cited in IRIS, 2003).

A sub-chronic (6-week) inhalation study of acetone vapours reported significant neurobehavioral effects in males exposed to 2,969 mg acetone/m^3 (Stewart *et al.*, cited in ATSDR, 1994). This LOAEL was used by the ATSDR to develop an intermediate and chronic inhalation MRL of 30 mg/m^3 for acetone. An uncertainty factor of 100 was applied to account for the use of a LOAEL (10) and for human variability (10). This MRL represents the ATSDR estimate of intermediate (greater than 14 days) and chronic (greater than a year) inhalation exposure to acetone at or below which a measurable risk of adverse, noncancerous effects is unlikely (ATSDR, 1994).

4.4.1.4 Carcinogenic Effects

Ott *et al.* (cited in ATSDR, 1994) conducted a retrospective mortality study of people exposed to acetone in their workplace (a cellulose fibre production plant); no significant risk of death due to malignant neoplasm was identified in association with acetone exposure.

4.4.1.5 Other Effects

No changes in cardiovascular, blood, or liver, parameters were reported in workers exposed to acetone in a cellulose fibre production plant (Ott *et al.*, cited in ATSDR, 1994).

4.4.2 Sub-Chronic Animal Effects

No chronic animal studies and only a few sub-chronic studies of acetone inhalation were identified (US EPA, 2003; ATSDR, 1994); this may be due to its low toxicity and endogenous availability (IPCS, 1998). Table 9 lists some of the lowest and highest NOAELs and LOAELs reported in the literature.

Table 9 NOAELs and LOAELs For Sub-Chronic Acetone Inhalation (Experimental Animals)

Effects Reported	Exposure Period	Air Concentration [b] ppm (mg Acetone/m^3)	Species	Reference
Systemic Effects:				
Respiratory; Cardiovascular; Hepatic; Renal. NOAEL.	3 hr/d, 5 d/wk, 2-8 wk	19,000 (45,134)	Rat	Bruckner and Peterson, cited in ATSDR, 1994 and IPCS, 1998.
Neurological:				
NOAEL.	3 hr/d, 5 d/wk, 2-8 wk	19,000 (45,134)	Rat	Bruckner and Peterson, cited in ATSDR, 1994.
Schedule-controlled operant behaviour (SCOB). NOAEL.	6h/d, 5 d/wk, 13 wk	4,000 (9,502)	Rat	CMA, cited in US EPA 2003.

[b] When both units of concentration were not provided in the literature, the following conversion factor and assumptions were used: mg/m^3 x 24.45/MW =ppm; MW=58.08, air at 25°C and 101.3 kPa (760mmHg) (Plog *et al.*, 1996).

No adverse effects were identified in a histological examination of lung, heart, and kidney tissues after high exposures (19,000 ppm or 45,134 mg/m^3) (Bruckner and Peterson, cited in ATSDR, 1994). Bruckner and Peterson (cited in ATSDR, 1994) also observed no changes in liver enzymes, liver weight, or liver histology after the same high does exposures. In this same study Bruchner and Peterson (cited in ATSDR, 1994) examined potential neurotoxic effects and reported a deceased total brain weight with no histologic changes. This indicates acetone's neurological effects are reversible (ATSDR, 1994).

4.4.2.1 Other Effects

Ingestion of high doses (50,000 ppm or 3,400 mg/kg body weight/day) produced mild testicular effects in rats; no reproductive effects were observed (Dietz *et al.*, Larson, NTP, cited in US EPA, 2003). No reproductive studies of chronic inhalation in animals were identified (US EPA, 2003).

4.5 Summary of Adverse Health Effects of Acetone Inhalation

The primary end points of toxicity associated with inhalation of acetone in humans and animals are respiratory tract and eye irritation, mood swings and nausea (IRIS, 2003; US EPA, 2003). Animal and human data indicate there may be potential neurobehavioural effects, which, if they occur, are mild and transient (U.S. EPA, 2003). It is important to note that very little chronic

inhalation data for humans and animals were identified (ATSDR, 1994; IPCS, 1998; IRIS, 2003, U.S. EPA, 2003). The ATSDR has established MRLs for acute and sub-chronic/chronic inhalation exposure to acetone. The US EPA and WHO determined there was insufficient animal or human data to calculate a chronic exposure limit for inhalation of acetone (IRIS, 2003; IPCS, 1998).

4.6 Effects on Vegetation

Little is known about the direct effects of volatile organic compounds (VOCs) on plants. Acetone has been demonstrated to be biogenic in nature and is released by both conifers and deciduous trees (Section 3.1.1). A search of ecological databases (*i.e.*, Web of Science, Biological Abstracts, Toxnet (available at http://toxnet.nlm.nih.gov/), and Ecotox (available at http://www.epa.gov/ecotox/)) was conducted for literature describing the effects of acetone on terrestrial and aquatic vegetation. The search resulted in the identification of only one research article on the subject.

Cape *et al.* (2003) evaluated the effect of a mixture of six VOCs on a number of herbaceous plants. These VOCs were acetone (200 $\mu g/m^3$) acetonitrile (6 $\mu g/m^3$), dichloromethane (6 $\mu g/m^3$), methylated spirits (ethanol) (30 $\mu g/m^3$), methyl *t*-butyl ether (20 $\mu g/m^3$), and toluene (12 $\mu g/m^3$). These six VOCs were selected on the basis of high annual tonnages, vapour pressures, persistence in the atmosphere, potential phytotoxicity, and hypro/lipophilicity. The levels of the VOCs were realistic atmospheric exposure at a given location in the United Kingdom. The plant species in the study were *Lotus corniculatus* L (birdsfoot trefoil), *Molinia caerulea* L. (purple moor grass), *Rumux obtusifolius* L (broadleaved dock), *Taraxacum officinale* L. (dandelion), *Trifolium prratense* L. (red clover), and *Viola tricolor* L. (common pansy). These plants were exposed to the VOC mixtures by open-top chambers for a period of 7 weeks. The VOC treatment resulted in significant effects on seed production in birdsfoot trefoil (12-fold increase of mean seed pod weight), a 21% increase of leaf water content in birdsfoot trefoil (calculated as a ratio of fresh weight to dry weight) and decreased photosynthetic efficiency in dandelion (18.4%) and red clover (5.5%), calculated as performance index.

The experimental design analyzed the effects of a mixture of VOCs likely to occur in the ambient UK atmosphere. While this study suggests that fairly low air concentrations of acetone (200 $\mu g/m^3$) may contribute to significant adverse effects in some plant species, these effects cannot be attributed specifically to acetone.

5.0 AIR SAMPLING AND ANALYTICAL METHODS

5.1 Reference Methods

Air sampling and analytical methods for acetone used in practice by established agencies are reported. In general, standard air monitoring methods for acetone are based on liquid impinger, coated-solid cartridge, sorbent tube, or direct-reading instrument sampling approaches. Widely employed and accepted reference air monitoring methods for acetone have been developed, tested and reported by the United States Environmental Protection Agency (US EPA), the National Institute of Occupational Safety and Health (NIOSH), and the Occupational Safety and Health Administration (OSHA). Refer to Table 10 for a description of individual method advantages and disadvantages.

5.1.1 US EPA Compendium Method TO-5

The US EPA has developed a number of methodologies suitable for sampling ambient air for trace-level concentrations of acetone. US EPA Compendium Method TO-5 describes the determination of individual aldehydes and ketones (including acetone) in ambient air using liquid impinger sampling followed by high performance liquid chromatography (HPLC) analysis with an ultraviolet (UV) detector (US EPA, 1999). Advantages of this method include: specific for aldehydes and ketones, good stability for derivative compounds formed in the impingers and low detection limits (*i.e.*, 1-50 ppbv). Disadvantages of this method include: acetone laboratory contamination is common, sensitivity limited by reagent purity, potential for evaporation of liquid over long term sampling, and isomeric aldehydes and ketones may be unresolved by the HPLC system.

This method uses a low volume pump to draw ambient air through a midget impinger containing a solution of dinitrophenylhydrazine (DNPH). The low volume pump is operated for 12 hours at a rate of 100 mL/min to collect a total volume of 72 L. After sampling, the impinger solution is placed in a screw-capped vial and returned to the laboratory for analysis. The DNPH derivatives are recovered by removing the isooctane layer, extracting the aqueous layer with 10 mL of 70/30 hexane/methylene chloride, and combining the organic layers. The combined organic layers are evaporated to dryness under a steam of nitrogen and the residue dissolved in methanol. The DNPH derivatives are determined using reversed phase HPLC with an UV adsorption detector operated at 370 nm.

5.1.2 US EPA Compendium Method TO-11A

The US EPA Compendium Method TO-11A describes the determination of formaldehyde and other carbonyl compounds (including acetone) in ambient air utilizing a DNPH coated-solid adsorbent followed by analysis with HPLC/UV detection (US EPA, 1999). The procedure is similar to US EPA Compendium Method TO-5 except that a coated silica gel cartridge is used instead of a liquid impinger. The advantages of this method include: placement of sorbent as first element in the sampling train minimizes contamination, sampling system is portable and lightweight, large database, and proven technology. Disadvantages of this method include: isometric aldehydes and ketones and other compounds with the same HPLC retention time may interfere, liquid water captured on the DNPH cartridge during sampling may interfere, carbonyls

on the DNPH cartridge may degrade if an ozone denuder is not employed, and ozone and UV light deteriorates trapped carbonyls on cartridge.

In this method, a known volume of ambient air is drawn through a prepackaged cartridge coated with acidified DNPH at a sampling rate of 100 to 2000 mL/min for an appropriate period of time. Sampling rate and time are dependent upon carbonyl concentration in the test atmosphere. After sampling, the sample cartridges and field blanks are individually capped and placed in shipping tubes with polypropylene caps. The capped tubes are placed in a polypropylene shipping container cooled to sub ambient temperature and returned to the laboratory for analysis. The cartridges are then removed from the vials and washed with acetonitrile by gravity feed elution. The eluate is diluted volumetrically and an aliquot is removed for determination of the DNPH-formaldehyde derivative by isocratic reverse phase HPLC with UV detection at 360 nm. Formaldehyde and other carbonyl compounds in the sample are identified and quantified by comparison of their retention times and peak heights or peak areas with those of standard solutions. Typically, carbonyl compounds are measured effectively to less than 0.5 ppbv.

5.1.3 US EPA Compendium Method TO-17

The US EPA Compendium Method TO-17 describes the determination of volatile organic compounds (VOCs) (including acetone) in ambient air using active sampling onto sorbent tubes (US EPA, 1999). This method is an alternative to the liquid impinger sampling method presented in Compendium Method TO-5 and to the coated-solid cartridge method presented in Compendium Method TO-11A. The advantages of this method include: placement of the sorbent as the first element minimizes contamination from other sample train components, large selection of sorbents to match with target analyte list, includes polar VOCs, better water management using hydrophobic sorbents, large database and proven technology, and size and cost advantages in sampling equipment. Disadvantages of this method include: distributed volume pairs required for quality assurance, rigorous clean-up of sorbent required, no possibility of multiple analysis, must purchase thermal desorption unit for analysis, desorption of some VOCs is difficult, and contamination of adsorbent can be a problem.

In this method, ambient air is actively drawn through a multi-bed sorbent tube where VOCs are trapped. The selection of tube and sorbent depends on the VOC in question. In the case of acetone, suitable commercially available sorbent tubes include: CSIII, C1000, Spherocarb 106 (SSV 1.5L) or Combination Tubes 2 or 3. A sampling apparatus with accommodations for two sampling tubes capable of independent control of sampling rates is used. For acetone, sampling rates of 16.7 mL/min and 66.7 mL/min are used to collect 1 and 4 L total sample volumes over a 1-hour period, respectively. The sorbent tube is returned to the laboratory where it is thermally desorbed and subsequently analyzed by gas chromatography with mass spectrometry detection (GC/MS) or other methods. This method applies to ambient concentrations of VOCs in the range of 0.5 to 25 ppbv.

5.1.4 US EPA Method 0030

The US EPA has also developed a method suitable for sampling gaseous emissions from a wide variety of stationary sources for the determination of trace-level concentrations of acetone. US EPA Method 0030 - Volatile Organic Sampling Train (VOST) describes the methodology for the collection of volatile principle organic hazardous constituents (POHCs) (including acetone) from

the stack gas effluents of hazardous waste incinerators (US EPA, 1986). For the purpose of definition, volatile POHCs are those POHCs with boiling points less than 100°C. This method employs a 20 L sample of effluent gas containing volatile POHCs that is withdrawn from a gaseous effluent source at a flow rate of 1 L/min, using a glass-lined probe and a VOST.

The gas stream is cooled to 20°C by passage through a water-cooled condenser and volatile POHCs are collected on a pair of sorbent resin traps. Liquid condensate is collected in an impinger placed between the two resin traps. The first resin trap (front trap) contains approximately 1.6 g of Tenax and the second trap (back trap) contains approximately 1 g each of Tenax and a petroleum-based charcoal, 3:1 by volume. A total of six pairs of sorbent traps may be used to collect volatile POHCs from the effluent gas stream. Analysis of the traps is carried out by thermal desorption purge-and-trap by GC/MS. The VOST is designed to be operated at 1 L/min with traps being replaced every 20 minutes for a total sampling time of 2 hours. Traps may be analyzed separately or combined onto one trap to improve detection limit. The target detection limit of this method is 0.1 to 100 $\mu g/m^3$ for selected POHCs collected on a set of sorbent traps using a total sample volume of 20 L or less.

5.1.5 NIOSH Method 1300

In addition to the air monitoring methods for acetone developed by the US EPA, both the NIOSH and the OSHA have also developed methods for acetone that are suitable for occupational, personal and area monitoring. The first methodology used by the NIOSH to determine acetone in air (NIOSH Method 1300) consists of collecting acetone on charcoal adsorption tubes with subsequent chemical analysis by gas chromatography with flame ionization detection (GC/FID) (NIOSH, 1994). Sampling is conducted by drawing air through a solid sorbent tube (coconut shell charcoal, 100 mg in the front section and 50 mg in the back section) using a personal sampling pump. The suggested flow rate is 0.01 to 0.2 L/min and the minimum volume collected should be 0.5 L and the maximum 3 L. The contents of the tube are desorbed with carbon disulphide and the desorbate is analyzed by GC/FID. The level of detection for concentrations of acetone using this method is 0.007 mg/L.

5.1.6 NIOSH Method 2549

A second methodology used by the NIOSH to determine acetone in air (NIOSH Method 2549) consists of collecting acetone in thermal desorption tubes with subsequent chemical analysis by GC/MS (NIOSH, 1996). Sampling is conducted by drawing air through a thermal desorption tube (*i.e.*, a multi-bed sorbent tube containing graphitized carbons and carbon molecular sieve sorbents) using a personal sampling pump. The suggested flow rate for acetone is 0.02 L/min with a volume collected of 5 L. The contents of the tube are thermally desorbed and the desorbate is analyzed by GC/MS. The level of detection for concentrations of acetone using this method is 100 ng or less.

5.1.7 NIOSH Method 3800

A final methodology used by the NIOSH to determine acetone in air (NIOSH Method 3800) consists of detecting concentrations of acetone using a portable direct-reading instrument using extractive Fourier Transform Infrared (FTIR) spectrometry (NIOSH, 2002). Sampling is conducted by drawing air through the instrument using a sampling pump at a flow rate of is

0.1 L/min to 20 L/min. The air is subsequently analyzed via FTIR spectrometry and the results displayed. The level of detection for concentrations of acetone using this method with a path length of 10 m is 0.95 ppmv with a maximum detectable concentration of 148 ppmv.

5.1.8 OSHA Method 69

OSHA has developed a fully validated method for the determination of acetone that is suitable for occupational, personal and area monitoring. The current methodology used by the OSHA to determine acetone in air (OSHA Method 39) was developed to be rapid, sensitive and precise (OSHA, 1988). This method consists of collecting acetone by drawing a known volume of air through standard sized sampling tubes (containing 130 mg of a carbon based molecular sieve absorbent in the front section and 65 mg in the back section) using a personal sampling pump. The suggested flow rate is 0.05 L/min and the recommended volume collected is 3 L after a sampling time of 1 hour. Samples are desorbed with dimethylformamide in carbon disulfide (in the presence of magnesium sulphate) and analyzed by GC/FID. The advantages of this method are a high sampling capacity and improved storage stability for acetone. The expense of the sampling tubes is a disadvantage of this procedure. The detection limit of the overall procedure is 2.0 ppmv or 4.7 mg/m^3 for a 3 L air sample. This is the amount of acetone spiked on the sampling device that allows recovery of an amount equivalent to the detection limit of the analytical procedure. The reliable quantitation limit is 2.0 ppmv or 4.7 mg/m^3. This is the smallest amount of acetone that can be quantified within the requirements of a recovery of at least 75% and a precision of ± 25% or better.

5.2 Alternative, Emerging Technologies

Reports, journal articles, conference proceedings and other sources known to contain information on ambient measurement methods for chemicals such as acetone were reviewed to determine the current status of alternative and emerging technologies. The results of the review indicate a general lack of technologies for ambient monitoring of acetone beyond the reference methods described earlier. A recent US EPA sponsored survey reinforces this by pointing out the need for methods development for chemicals such as acetone (Mukund *et al.*, 1995). Despite this need, several examples of alternative and emerging technologies have been developed and reported. In general, most non-standard methods and technologies are variations or modifications of those referenced methods previously mentioned. However, a few unique methods and technologies have been described, including passive and automated continuous sampling methods. Refer to Table 10 for a description of individual method advantages and disadvantages.

The most notable variations or modifications of reference methods for the collection and analysis of acetone involve alternative types of sorbents, reagents and sampling and analytical techniques to be used in conjunction with accepted approaches. Of the alternative sorbents, porous polymers, glass beads and glass fiber filters, XAD-2, Florisil, carbon (C_{18}) and silica gel are the most common (Vairavamurthy *et al.*, 1992). In addition, a new adsorbent high-surface-area graphitized carbon black (HSGCB) was found to be an interesting alternative to the usual sorbents used for sampling chemicals such as acetone (Mastrogiacomo *et al.*, 1998). Although the most widely used reagent continues to be DNPH, others, such as various hydrazines and hydroxylamines, have been proposed (Vairavamurthy *et al.*, 1992).

A number of modified sampling and analytical techniques based on standard methods have also been recommended. A new electrochromatography analytical method was developed for the separation and quantitation of aldehydes and ketones (including acetone) in ambient air (Fung and Long, 2001). In this method, air is sampled through a DNPH coated-solid cartridge in the field by a small air pump. The sample is subsequently desorbed and individual aldehydes and ketones are separated by electrochromatography and analyzed by mass spectrometry. This method can detect acetone in ambient air in concentrations as low as 0.041 $\mu g/m^3$. Amlathe and Gupta (1990) have developed a method whereby air is passed through a 1% sodium bisulphite solution and the absorbed acetone is reacted with an alkaline vanilla solution. Another method based on the reaction of mercuric oxide with carbonyl compounds and analysis by gas chromatography with reduction gas detection (GC/RGD) has been applied for the determination of low levels of acetone in unpolluted atmospheres (O'Hara and Singh, 1988). Campbell and Moore (1979) describe a method for detecting acetone in air that uses gas chromatography with nitrogen/phosphorous detection (GC/NPD) for analysis with sonication to increase the desorption efficiency. A cryotrapping sampling technique using glass traps cooled in liquid nitrogen for monitoring carbonyl compounds in air has also been developed (Levart and Verber, 2001). Other examples of alternative sampling and analytical techniques that have shown some promise in the detection of acetone include ultraviolet, 2-dimensional gas chromatographic, nebulization/reflux concentration, diode array and mass spectrometric detectors (Achatz *et al.*, 1999; Grosjean *et al.*, 1999; Sakuragawa *et al.*, 1999; Vairavamurthy *et al.*, 1992).

A number of passive samplers (diffusion tubes or gas badges) have been developed to measure concentrations of acetone in air as an alternative to the standard active pump sampling techniques. For passive sampling, the same collecting media (sorbent) as for active pump sampling can be used. The advantages of these samplers are that there are no moving parts to break down, regular flow calibration is unnecessary, and no bulky, expensive pumps are required. The badge or tube is exposed to ambient conditions for a set period of time (usually a much longer period than for active pump sampling) and then analyzed by an appropriate analytical method (Brown and Wright, 1994; Levin and Lindahl, 1994). Uchiyama and Hasegawa (1999) have developed a diffusive sampling device for organic carbonyl compounds (including acetone) which is suitable for the collection and analysis of low ppbv concentration levels. This sampling device is composed of three parts, an exposure part made of a porous polytetrafluoroethylene (PPTFE) tube, an analysis part made of polypropylene tubing and an absorbent part made of DNPH coated silica gel. Acetone is absorbed by the DNPH and subsequently detected by HPLC/UV. Another example of a tube-type passive sampler has been reported which employs a dansylhydrazine (DNSH)-coated solid sorbent for the collection of acetone and a sensitive HPLC-fluorescence technique for its detection (Zhang *et al.*, 2000). This device can detect levels of aldehydes and ketones in the range from 0.4 to 1.6 ppbv. The World Health Organization (IPCS, 1998) describes a passive dosimeter (badge) in which acetone is adsorbed on a porous polymer (Porapak-N) contained in a removable element and determined by thermal desorption with GC/FID detection. It can be used satisfactorily for determining acetone concentrations in air under a range of atmospheric conditions, when working to a control limit of 0.01 ppmv.

Automated continuously recording devices have recently been developed and utilized for monitoring atmospheric concentrations of acetone. Li *et al.* (2002) describe an Open Path

Fourier Transform Infrared (OP-FTIR) spectroscopy system that utilizes a beam of infrared light to detect path integrated concentrations of chemicals such as acetone along the beam path of the source and detector. It requires no sampling or sample handling, no prior knowledge of anticipated species and the spectral fingerprint of species are detected simultaneously. OP-FTIR integrates the concentrations over the infrared beam path and provides continuous real-time concentration information typically in durations of a few seconds. An automated measurement system for aldehydes and ketones (including acetone) using a diffusion scrubber in combination with HPLC was developed (Komazaki *et al.*, 1998; Possanzini *et al.*, 1996). Acetone is effectively collected by the diffusion scrubber, which consists of a hydrophobic porous tube disposed concentrically within a Pyrex-glass tube and a DNPH scrubbing solution. After the collection of the gas sample, the sample solution in the diffusion scrubber is injected into the HPLC system and individual species are separated and determined. All measurement operations are sequenced by a programmable controller which allows automated continuous measurement to be performed at 10-minute intervals. Automated continuously recording instruments with fast response times offer the best solution for monitoring average concentrations accurately, but most are bulky and expensive. In addition, many instruments are either insufficiently sensitive or selective in their measurements. The current focus of research relating to ambient acetone detection is on the development and testing of automated continuous sampling devices.

Table10 Advantages and Disadvantages of Sampling and Analytical Methods

Method	Advantages	Disadvantages
US EPA TO-5	Specific for aldehydes and ketones Good stability for derivative compounds formed in the impingers Low detection limits (*i.e.*, 1-50 ppbv)	Acetone laboratory contamination is common Sensitivity limited by reagent purity Potential for evaporation of liquid over long term sampling Isomeric aldehydes and ketones may be unresolved by the HPLC system
US EPA TO-11A	Placement of sorbent as first element in the sampling train minimizes contamination Sampling system is portable and lightweight Large database Proven technology	Isometric aldehydes and ketones and other compounds with the same HPLC retention time may interfere Liquid water captured on the DNPH cartridge during sampling may interfere Carbonyls on the DNPH cartridge may degrade if an ozone denuder is not employed Ozone and UV light deteriorates trapped carbonyls on cartridge
U.S. EPA TO-17	Minimises contamination Large selection of sorbents available Allows analysis for polar VOCs Better water management Large database and proven technology Equipment size and cost	Distributed volume pairs required for quality assurance Rigorous clean-up required No possibility of multiple analysis Require thermal desorption unit Desorption of some VOCs difficult Contamination of adsorbent possible
U.S. EPA Method 0030 NIOSH Method 1300 NIOSH Method 2549 NIOSH Method 3800	NA NA NA NA	NA NA NA NA
OSHA Method 69	High sampling capacity Improved storage stability Rapid, sensitive and precise	Sampling tubes are expensive
Alternative Sorbent Types	NA	NA
Alternative Analytical Techniques	High resolution and lower detection limits Rapid and efficient Capable of handling small sample size	NA
Passive Samplers	No moving parts to break down Regular flow calibration unnecessary No bulky, expensive pumps required As reliable as conventional methods	Only reliable at higher ambient concentrations Long exposure times required
Direct and continuous samplers	Reliable at low concentrations Fast response times Accurate	Bulky and expensive Complicated operation Many are insufficiently sensitive or selective

*NA denotes not available.

6.0 AMBIENT GUIDELINES OR OBJECTIVES

Current and/or recommended and proposed ambient guidelines and objectives of other jurisdictions in Canada, United States, and elsewhere were reviewed for acetone. All jurisdictions have specific uses for their guidelines. These uses may include:

- Reviewing permit applications for sources that emit air pollutants to the atmosphere;
- Investigating accidental releases or community complaints about adverse air quality for the purpose of determining follow-up or enforcement activity, and;
- Determining whether to implement temporary emission control actions under persistent adverse air quality conditions of a short-term nature.

6.1 Acetone Air Quality Guidelines and Objectives

Air quality guidelines and objectives for acetone are summarized in Table 11. Further details on the development and use of these guidelines or objectives by each jurisdiction are provided in Appendix A. The principal approaches by which guidelines and objectives are developed involve using an occupational exposure limit (OEL) and dividing it by safety or adjustment factors. A common OEL used by state agencies is the American Conference of Governmental Industrial Hygienists (ACGIH, 2003) 8-hour time weighted average (TWA) OEL of 1,780 mg/m^3. Another OEL commonly used is the National Institute for Occupational Safety and Health (NIOSH, 2003) relative exposure level (REL) of 590 mg/m^3.

The safety or adjustment factors are intended to account for issues such as: differences between eight-hour exposures in the workplace and continuous 24-hour environmental exposures; increased susceptibility of some people in the general population versus the relatively healthy worker, and; uncertainty in the margin of safety provided in an occupational exposure limit.

6.1.1 Canada

The Ontario Ministry of the Environment (MOE) adopted an Ambient Air Quality Criterion (AAQC) of 48 mg/m^3 as a 24-hour guideline. Ontario MOE uses the same value for a maximum point of impingement (POI) guideline (48 mg/m^3) based on a 30-minute averaging time.

6.1.2 United States

The U.S. Agency for Toxic Substances and Disease Registry (ATSDR, 2003) adopted a chronic inhalation MRL of 30 mg/m^3 based on neurobehavioral effects in humans. Four states – Arizona, New Hampshire, Vermont, and Washington – used the American Conference of Governmental Industrial Hygienists (ACGIH, 2003) 8-hour time weighted average occupational exposure limit (OEL) of 1,780 mg/m^3 for development of their guidelines with corresponding averaging times ranging from 8 hours to greater than one year. Michigan and Texas used the National Institute for Occupational Safety and Health (NIOSH, 2003) relative exposure level (REL) of 590 mg/m^3 for development of their guidelines with corresponding averaging times ranging from 1 hour to greater than one year. One state – Arizona – used the ACGIH (2003) 15-minute short-term exposure limit (STEL) of 2,380 mg/m^3 for development of their 1-hour guideline.

6.1.3 International Agencies

The New Zealand Ministry of Environment and Ministry of Health, the Netherlands National Institute of Public Health (RIVM, 2001), and WHO (2000) do not have air quality criteria for acetone.

6.2 Use of Occupational Limits for Ambient Air Quality Guidelines

Although widely practiced, there are several limitations in the direct and indirect application of occupational limits for ambient air quality guidelines:

- Occupational limits are based on the information gathered in workplace, through experience from medical research and practice, from experimental human and animal studies, and from a combination of these sources. Often they are based upon averaged tolerated doses from actual repeated industrial exposures. In this respect, they would be considered very accurate at predicting human adverse health effects in industrial exposure situations.
- Occupational limits are determined for a population of workers who are essentially healthy and who fall within a working age group of about 17 to 65 years. These individuals are supposedly in the prime of life, and potentially less susceptible to the effects of hazardous substances than other members of the public. Individuals vary in sensitivity or susceptibility to hazardous substances; with the elderly and infants in general being more susceptible than healthy workers.
- For most substances, a worker during a normal work schedule (8 hours per day, 5 days per week) receives 40 hours of exposure per week with daily breaks and extended weekend periods in which the body may rid itself of the accumulated substances before elevated levels are reached. For a person living continuously in an environment containing such substances, however, these recovery periods do not exist.

For these reasons, agencies using occupational limits have a policy of adjusting them downward with the use of safety or adjustment factors to derive guidelines for environmental (ambient) settings. The occupational limits are considered surrogates for benchmark values for ambient exposures only because they tend to be based upon a large body of toxicological, epidemiological, and/or clinical evidence pertaining to human exposure (albeit in the workplace). Uncertainty exists in terms of whether too little (or too much) safety is inherent in ambient air guidelines developed from occupational limits.

Table 11 Summary of Air Quality Guidelines for Acetone

Agency	Guideline Title	Guideline Value [mg/m^3] Averaging Time:			
		1-hour	8-hour	24-hour	Annual
Ontario MOE (1999)	Ambient Air Quality Criterion (AAQC): Maximum point of impingement (POI) Guideline:	48 (30-min)		48	
ATSDR (2003)	Acute (1-14 day exposure) inhalation minimum risk level (MRL):			62	
	Chronic inhalation MRL:				30
US EPA (IRIS, 2003)	No guideline exists.				
Arizona DEQ (1999)	Ambient Air Quality Guideline (AAQG):	20		14	
California EPA (1999); CAPCOA, 1992; California OEHHA/ARB, 2001)	No guideline exists.				
Indiana DEM (2002)	No guideline exists.				
Louisiana DEQ (current)	No guideline exists.				
Massachusetts DEP (1995)	Threshold Effects Exposure Limit (TEL):			0.16	
	Allowable Ambient Limit (AAL):				0.16
Michigan DEQ (2003)	Initial threshold screening level (ITSL):		5.9		
New Hampshire DES (current)	Ambient air limit (AAL):			4.2	2.8
New Jersey DEP (current)	No guideline exists.				
North Carolina ENR (current)	No guideline exists.				
Ohio EPA (2003; 1994)	No guideline exists.				
Oklahoma DEQ (2002)	No guideline exists.				
Rhode Island DEM (1992)	No guideline exists.				
Texas CEQ (TNRCC, 2001)	Effects screening level (ESL):	5.9			0.59
Vermont ANR (2001)	Hazardous ambient air standard (HAAS):		178		
Washington DOE(current)	Acceptable source impact level (ASIL):			5.9	
Wisconsin DNR (current)	No guideline exists.				
New Zealand MOE (2000)	No guideline exists.				
The Netherlands (RIVM, 2001)	No guideline exists.				
World Health Organization (2000)	No guideline exists.				

7.0 DISCUSSION

Establishing an ambient air quality guideline in the form of a concentration limit with a corresponding exposure duration (*i.e.*, averaging time) requires a number of factors to be taken into account, including:

- The nature of adverse health effects and conditions of exposure (*e.g.*, concentration and duration) associated with these effects;
- The estimated or actual degree of exposure of receptors, in particular those that may be sensitive to the air pollutant;
- The available technologies and associated economics for routinely or periodically monitoring for the pollutant in air, and;
- The availability and suitability of approaches for screening and estimating ambient ground-level concentrations in order to compare to the guidelines for permit applications or other situations.

Studies conducted by Environment Canada (1999) on ambient acetone indicated that air concentrations were well below acceptable levels within cities and near primary emission sources. This resulted in the removal of acetone as a reportable substance for Environment Canada's NPRI. Standard air monitoring methods for acetone are based on liquid impinger, coated-solid cartridge, sorbent tube, or direct-reading instrument sampling approaches. Widely employed and accepted reference air monitoring methods for acetone have been developed, tested and reported by the US EPA, NIOSH, and OSHA.

Ambient air guidelines in the form of short-term (acute) and long-term (chronic) duration are discussed below for acetone. Ideally, air quality guidelines serve to address exposures related to humans, animals, and vegetation. No direct exposure-related information was obtained for vegetation; therefore the discussion emphasizes the effects of acetone in human and animals.

7.1 Acute Exposure Conditions

In animal studies, acute lethal inhalation exposure to acetone concentrations ranging from 23,755 mg/m^3 (guinea pigs exposed for 48 hours) to 120,198 mg/m^3 (rats exposed for 3 hours) resulted in significant respiratory effects (decreased respiratory rate, pulmonary congestions, edema and hemorrhage of the lungs), cardiovascular effects, hepatic effects, neurological effects (narcosis) and ultimately death.

The highest NOAEL for pulmonary function or lung pathology following acute or sub-acute exposure was reported for mice exposed via inhalation to 14,253 mg acetone/m^3. A NOAEL of 5,226 mg/m^3 was reported in a study of developmental and hepatic effects in mice and rats as a result of acetone exposure (6 hours/day) for 14 days during gestation.

Adverse health effects reported in humans following acute (up to 24 hours) and sub-acute (up to one week) exposures to acetone via inhalation include: irritation of throat and nose ($\geq$ 236 mg/m^3); minor neurological disturbances (563 mg/m^3); minor alterations in haematological/ immunological parameters ($\geq$594 mg/m^3); and, shortened menstrual cycle

following repeated exposure (7.5 hours a day for 4 days) to high air concentrations (2,375 mg/m^3).

The ASTDR has established an acute inhalation minimum risk level (MRL) of 62 mg/m^3. The MRL was based on a LOAEL of 563 mg/m^3 for neurobehavioral disturbances (auditory discrimination) in humans, divided by a 9-fold uncertainty factor to account for the use of a minimal LOAEL (3-fold) and human variability (3-fold).

Provincial and state agencies that have developed acute air quality guidelines for acetone (averaging times of 24-hours or less) include Ontario MOE, Arizona DHS, Massachusetts DEP, Michigan DEQ, New Hampshire DES, Texas CEQ, Vermont ANR, and Washington DOE. With the exception of the 8-hour TWA guideline for Vermont (178 mg/m^3), all of the ambient air quality guidelines established for acute exposure to acetone were below the acute inhalation MRL (62 mg/m^3) recommended by the ATSDR (2003) for acute (1-14 days) exposure of the general public.

One-hour TWA guidelines for acetone have been established by Arizona and Texas. The Arizona 1-hour guideline of 20 mg/m^3 is based on the ACGIH 15-minute Short Term Exposure Limit (2,380 mg/m^3) divided by a safety factor of 120. In Texas, the 1-hour TWA guideline of 5.9 mg/m^3 is based on the NIOSH REL (590 mg/m^3) divided by a safety factor of 100.

Both Vermont and Michigan have 8-hour TWA guidelines for acetone. In Vermont, the guideline of 178 mg/m^3 was based on the ACGIH 8-hour TWA OEL (1,780 mg/m^3) divided by a safety factor of 10. Michigan established an 8-hour guideline of 5.9 mg/m^3 based on the NIOSH REL (590 mg/m^3) divided by a safety factor of 100.

The states of Arizona, Washington, and New Hampshire have all developed 24-hour TWA guidelines for acetone based on the ACGIH 8-hour TWA OEL (1,780 mg/m^3) divided by a safety factor. The Arizona 24-hour guideline of 14 mg/m^3 incorporates a safety factor of 126, the Washington State guideline of 5.9 mg/m^3 includes a 300-fold safety factor and the New Hampshire guideline of 4.2 mg/m^3 uses a safety factor of 420.

Massachusetts has established a 24-hour TWA guideline of 0.16 mg/m^3 for acetone, however, the basis for this air concentration was not reported. The Ontario 24-hour TWA guideline for acetone is 48 mg/m^3 and based on odour.

7.2 Chronic Exposure Conditions

Very little data on the effects of chronic exposure to acetone were identified, likely due to the low chronic toxicity and endogenous nature of acetone. In rats, no histological effects in lung, heart, kidney and liver tissues and no changes in liver enzymes were identified following sub-chronic exposure to 45,134 mg acetone/m^3 (3 hours/day, 5 days/week over 8 weeks).

An occupational exposure study reporting neurological effects in workers exposed to $\geq$1188 mg/m^3 acetone for 14 and 36 years was of limited use due to confounding exposure factors. However, a sub-chronic (6-week) inhalation study reported significant neurobehavioral

effects in males exposed to 2,969 mg acetone/m^3. This LOAEL was used by the ATSDR (2003) to develop an intermediate and chronic inhalation MRL of 30 mg/m^3. An uncertainty factor of 100 was applied to account for use of a LOAEL (10) and for human variability (10).

Agencies that have developed chronic air quality guidelines (annual average) for acetone include New Hampshire, Texas, and Massachusetts. The basis for the New Hampshire annual average guideline of 2.8 mg/m^3 is unknown. Texas established their annual average guideline of 0.59 mg/m^3 from the NIOSH REL (590 mg/m^3) divided by a safety factor of 1000. The Massachusetts annual average guideline of 0.16 mg/m^3 is equal to their 24-hour guideline; again, the basis for this air concentration was not reported.

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APPENDIX A
Air Quality Objectives for Acetone
Development and Use

Agency: Ontario Ministry of the Environment (OME).
Air Quality Guideline: Ambient Air Quality Criterion (AAQC) = 48,000 µg/m^3.
Averaging Time To Which Guideline Applies: 24-hour averaging time.
Basis for Development: Limiting effect based on odour.
Date Guideline Developed: Unknown.
How Guideline is Used in Practice: Used by Ontario Ministry of Environment (OME) to represent human health or environmental effect-based values not expected to cause adverse effects based on continuous exposure.
Additional Comments: AAQC is not used by OME to permit stationary sources that emit acetone to the atmosphere. A "point of impingement" standard is used to for permitting situations.
Reference and Supporting Documentation: Ontario Ministry of the Environment. 1999. Summary of Point Of Impingement Standards, Point Of Impingement Guidelines, and Ambient Air Quality Criteria (AAQC). Standards Development Branch, Ontario Ministry of the Environment, Toronto, ON. November 1999. 12 pp.

Agency: Ontario Ministry of the Environment (OME).
Air Quality Guideline: Maximum point of impingement (POI) Guideline = 48,000 $\mu g/m^3$.
Averaging Time To Which Guideline Applies: 30-minute averaging time.
Basis for Development: Not stated.
Date Guideline Developed: Unknown.
How Guideline is Used in Practice: Used by OME to review permit applications for stationary sources that emit acetone to the atmosphere.
Additional Comments: n/a
Reference and Supporting Documentation: Ontario Ministry of the Environment. 1999. Summary of Point Of Impingement Standards, Point Of Impingement Guidelines, and Ambient Air Quality Criteria (AAQC). Standards Development Branch, Ontario Ministry of the Environment, Toronto, ON. November 1999. 12 pp.

Agency: US Agency for Toxic Substances and Disease Registry (ATSDR).
Air Quality Guideline: Acute inhalation minimum risk level (MRL) = 61,780 µg/m^3 (26,000 ppb). Intermediate inhalation MRL = 30,890 µg/m^3 (13,000 ppb). Chronic inhalation MRL = 30,890 µg/m^3 (13,000 ppb).
Averaging Time To Which Guideline Applies: Acute inhalation minimum risk level (MRL): ≤14 continuous exposure Intermediate inhalation MRL: 15 to 364 days continuous exposure. Chronic inhalation MRL: 365 days and longer (i.e. continuous exposure over a lifetime).
Basis for Development: Acute inhalation MRL of 61,780 µg/m^3 (26,000 ppb) is based on a LOAEL of 237 ppm for neurobehavioral effects (auditory discrimination) in humans. The LOAEL was divided by an uncertainty factor of 9 (3 for use of a minimal LOAEL and 3 for human variability). The intermediate/chronic inhalation MRL of 30,890 µg/m^3 (13,000 ppb) is based on a LOAEL of 1,250 ppm for neurobehavioral effects in humans. The LOAEL was divided by an uncertainty factor of 100 (10 for use of a LOAEL and 10 for human variability).
Date Guideline Developed: Unknown.
How Guideline is Used in Practice: MRLs are intended to serve as a screening tool to help public health professionals decide where to look more closely. Inhalation MRLs are exposure concentrations that, based on current information, might cause adverse health effects in the people most sensitive to such substance-induced effects for exposure durations described above.
Additional Comments: Inhalation MRLs provide a basis for comparison with levels that people might encounter in air. If a person is exposed to acetone at an amount below the MRL, it is not expected that harmful (noncancer) health effects will occur. Because these levels are based only on information currently available, some uncertainty is always associated with them. Also, because the method for deriving MRLs does not use any information about cancer, an MRL does not imply anything about the presence, absence, or level of risk for cancer.
Reference and Supporting Documentation: Agency for Toxic Substances and Disease Registry (ATSDR). 2003. Minimal Risk Levels (MRLs) for Hazardous Substances. ATSDR, Public Health Service, US Department of Health and Human Services. Atlanta, GA. http://www.atsdr.cdc.gov/mrls.html (accessed Oct. 6, 2003).

Agency: US Environmental Protection Agency (EPA).
Air Quality Guideline: US EPA does not have an air quality guideline for this chemical.
Averaging Time To Which Guideline Applies: n/a
Basis for Development: n/a
Date Guideline Developed: n/a
How Guideline is Used in Practice: n/a
Additional Comments: n/a
Reference and Supporting Documentation: US Environmental Protection Agency. Integrated Risk Information System. http://www.epa.gov/iris/ (accessed 4 October 2003).

Agency:

Arizona Department of Health Services (DHS).

Air Quality Guideline:

Arizona Ambient Air Quality Guidelines (AAAQGs):

1-hour AAAQG = 20,000 $\mu g/m^3$.

24-hour AAAQG = 14,000 $\mu g/m^3$.

Averaging Time To Which Guideline Applies:

See above.

Basis for Development:

The 1-hour AAAQG is derived by taking the American Conference of Governmental Industrial Hygienists (ACGIH) 15-minute Short Term Exposure Limit (STEL) of 2,380 mg/m^3 and dividing it by a factor of 120. The factor of 120 converts a 15-minute exposure into a one-hour exposure, and includes a safety factor of 30 to protect the most sensitive members of the population such as children and the elderly.

The 24-hour AAAQG is derived by taking the ACGIH 8-hour TWA occupational exposure limit (OEL) of 1,780 mg/m^3 and dividing it by a factor of 126. The factor of 126 incorporates the conversion of an 8-hour, 5-day work week to a 24-hour, 7-day week of 4.2, and a safety factor of 30 to protect the most sensitive members of the population such as children and the elderly.

Date Guideline Developed:

Unknown.

How Guideline is Used in Practice:

AAAQGs are not intended to be used as standards. Rather, they are intended to provide health-based guidelines that may be useful in making environmental risk management decisions. AAAQGs consider human health risk from inhalation of contaminants in ambient air. They do not take into account odour thresholds or threats to wildlife.

Additional Comments:

AAAQGs are residential screening values that are protective of human health, including children. Chemical concentrations in air that exceed AAAQGs may not necessarily represent a health risk. Rather, when contaminant concentrations exceed these guidelines, further evaluation may be necessary to determine whether there is a true threat to human health.

Reference and Supporting Documentation:

Arizona Department of Health Services (DHS). 1999. 1999 Update – Arizona Ambient Air Quality Guidelines (AAAQGs). Report prepared for Arizona Department of Environmental Quality, Air Programs Division. Arizona DHS, Office of Environmental Health, Phoenix, AZ. 11 May 1999. 20 pp.

Agency: California Environmental Protection Agency (Cal EPA).
Air Quality Guideline: Cal EPA does not have an air quality guideline for this chemical.
Averaging Time To Which Guideline Applies: n/a
Basis for Development: n/a
Date Guideline Developed: n/a
How Guideline is Used in Practice: n/a
Additional Comments: n/a
Reference and Supporting Documentation: California Environmental Protection Agency (Cal EPA). 1999. Determination of Acute Reference Exposure Levels for Airborne Toxicants. Office of Environmental Health Hazard Assessment, Air Toxicology and Epidemiology Section, Cal EPA. Oakland, CA. March 1999. California Air Pollution Control Officers Association (CAPCOA). 1992. Air Toxics "Hot Spots" Program Risk Assessment Guidelines, Prepared by AB2588 Risk Assessment Committee of CAPCOA, Sacramento, CA. January 1992. California Office of Environmental Health Hazard Assessment (OEHHA)/Air Resources Board (ARB). 2001. Approved Chronic Reference Exposure Levels and Target Organs. Table 3 (last updated 13 September 2001). Available at: www.arb.ca.gov/toxics/healthval/chronic.pdf (accessed 5 October 2003).

Agency: Indiana Department of Environmental Management (IDEM).
Air Quality Guideline: IDEM does not have an air quality guideline for this chemical.
Averaging Time To Which Guideline Applies: n/a
Basis for Development: n/a
Date Guideline Developed: n/a
How Guideline is Used in Practice: n/a
Additional Comments: n/a
Reference and Supporting Documentation: Indiana Department of Environmental Management (DEM). 2002. Office of Air Quality Programs. Indiana DEM, Office of Air Quality. Indianapolis, IN. Available at: http://www.in.gov/idem/air/programs/modeling/policy.html (accessed 5 October 2003).

Agency: Louisiana Department of Environmental Quality (DEQ).
Air Quality Guideline: Louisiana DEQ does not have an air quality guideline for this chemical.
Averaging Time To Which Guideline Applies: n/a
Basis for Development: n/a
Date Guideline Developed: n/a
How Guideline is Used in Practice: n/a
Additional Comments: n/a
Reference and Supporting Documentation: *Louisiana Administrative Code (LAC). Title 33 Environmental Quality, Part III Air, Chapter 51. Comprehensive Toxic Air Pollutant Emission Control Program. Louisiana Department of Environmental Quality. Baton Rouge, LA.*

Agency: Massachusetts Department of Environmental Protection (DEP).
Air Quality Guideline: Threshold Effects Exposure Limit (TEL) = 160.54 (160) µg/m^3 [24-hour averaging time]. Allowable Ambient Limit (AAL) = 160.54 (160) µg/m^3 [annual average].
Averaging Time To Which Guideline Applies: See above.
Basis for Development: Unknown.
Date Guideline Developed: Unknown.
How Guideline is Used in Practice: Information could not be obtained to identify how the guideline is used in practice, but it is expected that the guideline is used in some manner to meet state level permitting.
Additional Comments: n/a
Reference and Supporting Documentation: Massachusetts Department of Environmental Protection (DEP). 1995. Revised air guidelines [updated list of 24-hour average Threshold Effects Exposure Limit (TEL) values and annual average Allowable Ambient Limit (AAL) values]. Massachusetts DEP, Boston, MA. 6 December 1995. Memorandum available at: http://www.state.ma.us/dep/ors/files/aallist.pdf (accessed 5 October 2003).

Agency: Michigan Department of Environmental Quality (DEQ).
Air Quality Guideline: Initial threshold screening level (ITSL) = 5,900 $\mu g/m^3$.
Averaging Time To Which Guideline Applies: 8-hour averaging time.
Basis for Development: Based on the National Institute for Occupational Safety and Health (NIOSH) relative exposure level (REL) of 590 mg/m^3 for acetone divided by a safety factor of 100.
Date Guideline Developed: 1992.
How Guideline is Used in Practice: There are two basic requirements of Michigan air toxic rules. First, each source must apply the best available control technology for toxics (T-BACT). After the application of T-BACT, the emissions of the toxic air contaminant cannot result in a maximum ambient concentration that exceeds the applicable health based screening level for non-carcinogenic effects (ITSL). Application of an ITSL is required for any new or modified emission source or sources for which a permit to install is requested and which emits a toxic air contaminant.
Additional Comments: The applicable air quality screening level for chemical treated as non-carcinogens by Michigan DEQ is the ITSL. There are two health based screening levels for chemical treated as carcinogens by Michigan DEQ: the initial risk screening level (IRSL) – based on an increased cancer risk of one in one million, and the secondary risk screening level (SRSL) – based on as an increased cancer risk of 1 in 100,000.
Reference and Supporting Documentation: *Michigan Administrative Code (MAC). Air Pollution Control Rules. Part 2 Air Use Approval, R 336.1201 - 336.1299. Air Quality Division, Department of Environmental Quality. Lansing, MI.*

Agency: New Hampshire Department of Environmental Services (DES).
Air Quality Guideline: 24-hour ambient air limit (AAL) = 4,243 µg/m^3. Annual ambient air limit (AAL) = 2,829 µg/m^3.
Averaging Time To Which Guideline Applies: See above.
Basis for Development: The AALs were developed in the following manner: 24-hour Ambient Air Limit – The American Conference of Governmental Industrial Hygienists (ACGIH) 8-hour time weighted average occupational exposure limit (OEL) of 750 ppm (1,780 mg/m^3) is divided by a safety factor (SF) of 100 and a time adjustment factor (TAF) of 4.2. Annual Ambient Air Limit – Unknown.
Date Guideline Developed: Unknown.
How Guideline is Used in Practice: AALs are used by New Hampshire DES to review permit applications for sources that emit acetone to the atmosphere. Sources are regulated through a statewide air permitting system and include any new, modified or existing stationary source, area source or device.
Additional Comments: n/a
Reference and Supporting Documentation: *New Hampshire Administrative Rule. Chapter Env-A 1400. Regulated Toxic Air Pollutants. New Hampshire Department of Environmental Services. Concord, NH.*

Agency: New Jersey Department of Environmental Protection (DEP).
Air Quality Guideline: Applicants are required to carry out a risk assessment in conjunction with applying for an air pollution control pre-construction permit. New Jersey DEP normally uses US EPA toxicological criteria from the Integrated Risk Information System. In the case of acetone, US EPA does not have inhalation toxicological criteria so it is unknown how New Jersey DEP treats acetone.
Averaging Time To Which Guideline Applies: n/a
Basis for Development: n/a
Date Guideline Developed: n/a
How Guideline is Used in Practice: n/a
Additional Comments: n/a
Reference and Supporting Documentation: *New Jersey Administrative Code (NJAC). Title 7, Chapter 27, Subchapter 8. Permits and Certificates for Minor Facilities (and Major Facilities without an Operating Permit). New Jersey Department of Environmental Protection. Trenton, NJ.* New Jersey Department of Environmental Protection. 1994. Technical Manual 1003. Guidance on Preparing a Risk Assessment for Air Contaminant Emissions. Air Quality Permitting Program, Bureau of Air Quality Evaluation, New Jersey Department of Environmental Protection. Trenton, NJ. Revised December 1994.

Agency: North Carolina Department of Environment and Natural Resources (ENR).
Air Quality Guideline: North Carolina ENR does not have an air quality guideline for acetone.
Averaging Time To Which Guideline Applies: n/a
Basis for Development: n/a
Date Guideline Developed: n/a
How Guideline is Used in Practice: n/a
Additional Comments: n/a
Reference and Supporting Documentation: *North Carolina Administrative Code (NCAC). North Carolina Air Quality Rules 15A NCAC 2D.1100 – Air Pollution Control Requirements (Control of Toxic Air Pollutants). North Carolina Department of Environment and Natural Resources. Raleigh, NC.* *North Carolina Administrative Code (NCAC). North Carolina Air Quality Rules 15A NCAC 2Q.0700 – Air Quality Permit Procedures (Toxic Air Pollutant Procedures). North Carolina Department of Environment and Natural Resources. Raleigh, NC.*

Agency: Ohio Environmental Protection Agency (EPA).
Air Quality Guideline: Ohio EPA does not have an air quality guideline for acetone.
Averaging Time To Which Guideline Applies: n/a
Basis for Development: n/a
Date Guideline Developed: n/a
How Guideline is Used in Practice: n/a
Additional Comments: n/a
Reference and Supporting Documentation: Ohio Environmental Protection Agency (EPA). 2003. Review of New Sources of Toxic Emissions. Air Toxics Unit, Division of Air Pollution Control, Ohio EPA. Columbus, OH. 11 pp (available at: http://www.epa.state.oh.us/dapc/atu/atu.html, accessed 5 October 2003). Ohio Environmental Protection Agency (Ohio EPA). 1994. Review of New Sources of Air Toxic Emissions. Proposed for Public Comment. Division of Air Pollution Control, Ohio EPA. Columbus, OH. January 1994. 31 pp.

Agency: Oklahoma Department of Environmental Quality (DEQ).
Air Quality Guideline: Oklahoma DEQ does not have an air quality guideline for acetone.
Averaging Time To Which Guideline Applies: n/a
Basis for Development: n/a
Date Guideline Developed: n/a
How Guideline is Used in Practice: n/a
Additional Comments: n/a
Reference and Supporting Documentation: *Oklahoma Administrative Code (OAC). Title 252. Chapter 100. Air Pollution Control. 100:252-41 - Control of Emission of Hazardous and Toxic Air Contaminants. Oklahoma Department of Environmental Quality. Oklahoma City, OK.* Oklahoma Department of Environmental Quality (DEQ). 2002. Air Toxics Partial Listing [maximum acceptable ambient concentrations (MAAC) for air toxics]. Oklahoma City, OK. Available at: http://www.deq.state.ok.us/AQDNew/toxics/listings/pollutant_query_1.html (accessed 5 October 2003).

Agency: Rhode Island Department of Environmental Management (DEM).
Air Quality Guideline: Rhode Island DEM does not have an air quality guideline for acetone.
Averaging Time To Which Guideline Applies: n/a
Basis for Development: n/a
Date Guideline Developed: n/a
How Guideline is Used in Practice: n/a
Additional Comments: n/a
Reference and Supporting Documentation: *Rhode Island Department of Environmental Management. 1992. Air Pollution Control Regulation No. 22. Division of Air and Hazardous Materials, Rhode Island Department of Environmental Management. Providence, RI. Amended 19 November 1992.*

Agency: Texas Commission on Environmental Quality (CEQ) – formerly Texas Natural Resource Conservation Commission (TRNCC).
Air Quality Guideline: Short-term effects screening level (ESL) = 5,900 $\mu g/m^3$. Long-term effects screening level (ESL) = 590 $\mu g/m^3$.
Averaging Time To Which Guideline Applies: 1-hour averaging time for short-term ESL. Annual averaging time for long-term ESL.
Basis for Development: Short-term Effects Screening Level – The National Institute for Occupational Safety and Health (NIOSH) relative exposure level (REL) of 590 mg/m^3 for acetone is divided by a safety factor of 100. Long-term Effects Screening Level – The National Institute for Occupational Safety and Health (NIOSH) relative exposure level (REL) of 590 mg/m^3 for acetone is divided by a safety factor of 1000.
Date Guideline Developed: Not stated.
How Guideline is Used in Practice: ESLs are used to evaluate the potential for effects to occur as a result of exposure to concentrations of constituents in air. ESLs are based on data concerning health effects, odour nuisance potential, effects with respect to vegetation, and corrosion effects. They are not ambient air standards. If predicted or measured airborne levels of a chemical do not exceed the screening level, adverse health or welfare effects would not be expected to result. If ambient levels of constituents in air exceed the screening levels, it does not necessarily indicate a problem, but rather, triggers a more in-depth review.
Additional Comments: n/a
Reference and Supporting Documentation: Texas Natural Resource Conservation Commission (TNRCC) 2001. Toxicology & Risk Assessment (TARA) Section Effects Screening Levels. http://www.tnrcc.state.tx.us/permitting/tox/index.html (accessed 13 October 2003).

Agency: Vermont Agency of Natural Resources (ANR).
Air Quality Guideline: Hazardous ambient air standard (HAAS) = 178,000 $\mu g/m^3$.
Averaging Time To Which Guideline Applies: 8-hour averaging time.
Basis for Development: The HAAS is equivalent to the American Conference of Governmental Industrial Hygienists (ACGIH) 8-hour time weighted average occupational exposure limit (OEL) of 1,780 mg/m^3 divided by a safety factor (SF) of 10.
Date Guideline Developed: Not stated.
How Guideline is Used in Practice: HAASs are used by Vermont ANR to review permit applications for stationary sources that emit acetone to the atmosphere.
Additional Comments: n/a
Reference and Supporting Documentation: Appendix C - Rule 5-261 - Control of Hazardous Air Contaminants, Vermont Air Pollution Control Regulations. 2001. State of Vermont Agency of Natural Resources. Air Pollution Control Division. Waterbury, VT. 29 November 2001. 187 pp.

Agency: Washington State Department of Ecology (DOE).
Air Quality Guideline: Acceptable source impact level (ASIL) = 5,900 $\mu g/m^3$.
Averaging Time To Which Guideline Applies: 24-hour averaging time.
Basis for Development: The ASIL is equivalent to the American Conference of Governmental Industrial Hygienists (ACGIH) 8-hour time weighted average occupational exposure limit (OEL) of 1,780 mg/m^3 divided by a safety factor (SF) of 300 and rounded.
Date Guideline Developed: Unknown.
How Guideline is Used in Practice: ASILs are used by Washington State DOE to review permit applications for sources that emit acetone to the atmosphere.
Additional Comments: n/a
Reference and Supporting Documentation: *Washington Administrative Code (WAC). Chapter 173-460 WAC. Controls For New Sources Of Toxic Air Pollutants. Washington State Department of Ecology. Olympia, WA.*

Agency: Wisconsin Department of Natural Resources (DNR).
Air Quality Guideline: Wisconsin DNR does not have an air quality guideline for acetone.
Averaging Time To Which Guideline Applies: n/a
Basis for Development: n/a
Date Guideline Developed: n/a
How Guideline is Used in Practice: n/a
Additional Comments: n/a
Reference and Supporting Documentation: *Wisconsin Administrative Code (WAC). Air Pollution Control Rules. Chapter NR 445. Control of Hazardous Pollutants. Wisconsin Department of Natural Resources. Madison WI.*

Agency: New Zealand Ministry for the Environment (MOE) and New Zealand Ministry of Health (MOH).
Air Quality Guideline: New Zealand MOE and MOH does not have air quality criteria for acetone.
Averaging Time To Which Guideline Applies: n/a
Basis for Development: n/a
Date Guideline Developed: n/a
How Guideline is Used in Practice: n/a
Additional Comments: n/a
Reference and Supporting Documentation: New Zealand Ministry for the Environment and Ministry of Health (New Zealand). 2000. Proposals for Revised and New Ambient Air Quality Guidelines. Discussion Document. Air Quality Technical Report No 16. Prepared by the Ministry for the Environment and the Ministry of Health. December 2000. 79 pp.

Agency: The Netherlands National Institute of Public Health and the Environment (RIVM)
Air Quality Guideline: RIVM does not have air quality criteria for acetone.
Averaging Time To Which Guideline Applies: n/a
Basis for Development: n/a
Date Guideline Developed: n/a
How Guideline is Used in Practice: n/a
Additional Comments: n/a
Reference and Supporting Documentation: The Netherlands National Institute of Public Health and the Environment (RIVM). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVN Report 711701 025. RIVN, Bilthoven, The Netherlands. March 2001. 297 pp.

Agency: World Health Organization (WHO)
Air Quality Guideline: WHO does not have air quality criteria for acetone.
Averaging Time To Which Guideline Applies: n/a
Basis for Development: n/a
Date Guideline Developed: n/a
How Guideline is Used in Practice: n/a
Additional Comments: n/a
Reference and Supporting Documentation: World Health Organization (WHO). 2000. Air Quality Guidelines for Europe, 2nd Edition. WHO Regional Publications, European Series, No. 91. WHO Regional Office for Europe, Copenhagen. 273 pp